CADTH REIMBURSEMENT REVIEW

Patient and Clinician Group Input

Pemigatinib (Pemazyre)

Incyte Biosciences Canada Corporation

Indication: Pemazyre (pemigatinib) for the treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a FGFR2 fusion or other rearrangement.

December 13, 2024

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CADTH in all phases of the review, including the appraisal of evidence and interpretation of the results. The input submitted for each review is also included in the briefing materials that are sent to expert committee members prior to committee meetings.

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CADTH

Patient Input Template for CADTH Reimbursement Reviews

Name of Drug:	Pemazyre (pemigatinib)
Indication:	For the treatment of adults with previously treated, unresectable locally advanced or metastatic CCA with an FGFR2 fusion or other rearrangement
Name of Patient Group:	Cholangio-Hepatocellular Carcinoma Canada (CHCC) collectively with: • Colorectal Cancer Resource & Action Network (CCRAN) • Canadian Cancer Survivor Network (CCSN) • Canadian Cholangiocarcinoma Collaborative (C3) • Gastrointestinal Society (GI Society)
Author of Submission:	Brenda Clayton, President & CEO, CHCC [redacted] [redacted]

1. About Your Patient Group

Cholangio-Hepatocellular Carcinoma Canada **(CHCC)** is a national, not-for-profit patient support and advocacy group championing the health and well-being of Canadians touched by cholangiocarcinoma and hepatocellular carcinoma and those at risk of developing these diseases. This HTA patient evidence submission serves cholangiocarcinoma patients within the oncology space.
CHCC assumed the lead on a collective patient input submission for Pemazyre as a second-line treatment following a first line course of chemotherapy for the treatment of adult patients with locally advanced, unresectable, or metastatic cholangiocarcinoma (CCA). The following patient advocacy groups thoughtfully collaborated with CHCC to ensure the advanced, unresectable or metastatic cholangiocarcinoma patient/caregiver perspective was captured, represented, and woven throughout this submission:

- Colorectal Cancer Resource & Action Network **(CCRAN)**
- Canadian Cancer Survivor Network **(CCSN)**
- Canadian Cholangiocarcinoma Collaborative **(C3)**
- Gastrointestinal Society **(GI Society)**

2. Information Gathering

In collaboration with the four patient advocacy groups, CHCC employed a multi-faceted outreach strategy to help collect, organize and present the cholangiocarcinoma patient/caregiver input.

On October 22, 2024, CHCC reached out via email to 5 Canadian clinicians who treat cholangiocarcinoma, 5 patients associated with CHCC and the three patient advocacy organizations (GI Society joined post outreach efforts), wherein we kindly requested assistance with patient/caregiver recruitment for CHCC's cholangiocarcinoma qualitative telephone and Zoom interviews. A flyer (**Appendix B**) was posted on CHCC's website, seeking patients with the lived experience with the drug under review. The flyer was also sent out to the collaborating organizations for posting on their respective websites. The call for patients across Canada to participate in a qualitative interview was also mentioned in the CTV News article on Pemazyre on November 6.

CHCC adapted and used a previously designed (and validated) qualitative questionnaire (with permission) by CCRAN. Telephone interviews were conducted, with each interview lasting approximately 60 minutes. The survey helped capture the advanced cholangiocarcinoma patient experience with the disease, currently available treatments, and the therapy under review. The telephone and Zoom interviews were administered between October 23, 2024, and November 7, 2024.

It is important to note that the patients have been receiving Pemazyre therapy for varying lengths of time. Three patients had difficulty obtaining the drug but did have the FGFR2 fusion mutation, hence, their lived experience with the drug under review was indeed included. Our collective efforts captured the values, priorities, and preferences of 12 patients who underwent the Pemazyre journey. In addition, the questionnaire includes the impact on the caregiver experience.

Patient demographics are included as follows:

Table 1: Respondent Demographics

Demographic/ Respondent	Age (@Dx)	Gender	Location
Patient A	62 (59)	Female	Newmarket, ON Canada
Patient B	56 (54)	Female	High River, AB Canada
Patient C	46 (44)	Female	Kelowna, BC Canada
Patient D	26 (24)	Female	Kitchener, ON Canada
Patient E	50 (48)	Female	Stettler, AB Canada
Patient F	43 (40)	Female	Blackie, AB Canada
Patient G	76 (74)	Female	Mississauga, ON Canada
Patient H	68 (62)	Female	Toronto, ON Canada
Patient I	79 (78)	Female	Barrie, ON Canada
Patient J	38 (31)	Female	Israel (Formerly Edmonton, AB, Canada)
Patient K	57 (55)	Male	Vernon, BC Canada
Patient L	45 (42)	Female	Grimsby, ON Canada

Our efforts generated twelve highly informed qualitative patient interviews as captured entirely in Appendix C.

Appendix C includes interviews with eleven participants across Canada (B.C., Alberta, and Ontario) and one from Israel. ***Patient J*** *is Canadian, and she stated,* **"I was living in Edmonton, Alberta and moved to Israel in 2020 so that I could get treatment that Canada did not offer."** The participants' ages ranged from 26 to 79 at the time of the interview. At diagnosis, they ranged from 24 to 78. The median age at diagnosis was 51 years. This is younger than the typical median age onset of 68 years (Reddy et al., 2023). One male and eleven females were interviewed.

- Three patients (A, I, & L) could not obtain Pemazyre the initial time they were interviewed; since then, two patients have obtained access with the Ontario government covering the cost, and the third person is still waiting on the paperwork to go through.
- Nine patients were able to obtain Pemazyre for varying amounts of time. Five patients (B, E, H, J, & K) did not have to pay for the drug out-of-pocket, obtaining Pemazyre through compassionate access or covered by their provincial government. Four patients had to pay for Pemazyre themselves, two through private insurance (C & F), one person was required to fundraise through a GoFundMe campaign (D), and one person paid for the drug out of their pocket (G).

These twelve patients' heart-wrenching testimonials are comprehensively incorporated into this submission to ensure the advanced, metastatic cholangiocarcinoma patient's voice is represented, and to help inform this committee's deliberations. **There is no Canadian-reimbursable first-line targeted therapy for CCA patients with the FGFR2 fusion mutation.** Patients who had coverage of Pemazyre were very thankful for the extension of their life as there is no other available treatment for this cancer after first-line chemotherapy. Their lived experience with this cancer and the treatment provided is extensive and impactful.

3. Disease Experience

Cholangiocarcinoma is a rare and aggressive cancer, often diagnosed in the late stages, with a poor prognosis (Neumann et al., 2022). Intrahepatic cholangiocarcinoma (iCCA) is the second most common liver malignancy (Tsilimigras et al., 2020). According to the Canadian Cancer Statistics, 730 people were diagnosed with cholangiocarcinoma in 2019, the year in which the latest statistics are available for Canada (Canadian Cancer Society, 2024). Approximately 15% of all hepatobiliary tumours are found to be intrahepatic cholangiocarcinoma (iCCA) in nature (Pascale et al., 2023). The global incidence of iCCA is increasing, and the prognosis remains poor, with a 5-year survival rate of 5%-20% (Neumann et al., 2022; Pascale et al., 2023; Brandi et al., 2024). If the disease is localized (has not spread beyond the liver), the 5-year survival rate is for iCCA 23%; if it is regional iCCA (close to or around the liver), the 5-year survival rate is 9%; and if it is distant (metastasized), the 5-year survival rate drops sharply to 3% (Canadian Cancer Society, 2024). Unfortunately, one patient who was interviewed succumbed to her disease after her interview and before the submission was completed.

Cholangiocarcinoma has three subtypes, depending on location: intrahepatic cholangiocarcinoma (iCCA), distal cholangiocarcinoma (dCCA), and perihilar cholangiocarcinoma (pCCA). The dCCA and the pCCA are often grouped together as extrahepatic cholangiocarcinoma (eCCA). Pemazyre targets an FGFR2 fusion mutation almost exclusively found in iCCA (Vogel et al., 2024).

Symptoms are often vague in the beginning, ranging from stomach upset, indigestion, and mild pain in the abdomen. By the time patients see their physician, they already have advanced disease. We heard this repeatedly from our interviewed patients. Diagnosis involves physical history and exam, blood work, liver function tests, CA19-9 tumour marker test, ultrasound, CT and MRI scans and biopsy (National Cancer Institute 2024). The patients interviewed were diagnosed as follows:

The interviewed patients accessed the following diagnostics to diagnose their cholangiocarcinoma:

- Ultrasound: 7 of 12
- Biopsy: 8 of 12
- Blood work: 4 of 12
- CT scan: 3 of 12
- MRI: 1 of 12
- PET scan: 1 of 12

The following patients describe their variable symptoms:

Patient A *stated*, **"In April 2022, I was experiencing stomach pains so bad that I went to the walk-in clinic in Newmarket. I had an ultrasound (U/S) immediately. They saw a mass and did a biopsy immediately. I also had blood work done."**

Patient E *stated,* **"I had weird, strange back pain that would come and go. I also had some indigestion. I went to see the doctor about it. I had an ultrasound in March 2023, which showed a 5cm mass in my liver."**

Patient I *had a different experience, in which she stated,* **"I was asymptomatic. It was the broken collarbone that brought me to hospital."** She said, "**… When I went to the hospital, it was picked up on the x-rays I had."**

Patient J *stated*, **"I had yearly PET scans since I was diagnosed with Wilson's disease in 2005. My liver is cirrhotic. I was asymptomatic. The scan picked up a 2cm tumour and my CA19-9 was high."**

Of the patients interviewed, for **Patients A, C, D, F, G, I, and K,** (**7 out of 12**), the cancer had already metastasized and never went away after diagnosis.

Thus, surgery with curative intent is only feasible for a few patients (Casadei-Gardini et al., 2023). However, the prognosis is still discouraging because 50%-70% of patients who have a resection will experience a disease recurrence (Tsilimigras et al., 2020).

Although **Patients B, E, H, J, and L** had liver resections, they **all** experienced recurrences and had to access chemotherapy.

There are a few genetic mutations or alterations in iCCA (Ramjeesingh et al., 2023). They include but are not exclusive to FGFR2 fusion, IDH1/IDH2 mutations, HER2 amplification, NTRK fusions, etc. (Ramjeesingh et al., 2023). Pemazyre targets the FGFR2 fusion mutation or alteration (biomarker).

All patients were tested for biomarkers at some point, and everyone had the FGFR2 fusion mutation.

The disease experience is closely linked to the experiences with currently available treatments because patients are placed on the standard of care chemotherapy almost as soon as they are diagnosed.

Patient A was diagnosed on May 6, 2022, and chemotherapy was initiated that month.
Patient B was diagnosed in late January 2023 and started chemotherapy in March 2023.
Patient C was diagnosed in November 2022 and began chemotherapy in December 2022.
Patient D was diagnosed in October 2022 and began chemotherapy in October 2022.
Patient E was diagnosed in April 2023 and had surgery in August 2023. She has an unusual case as she was diagnosed with 3 different cancers, but since cholangiocarcinoma is the most aggressive of the three cancers, the decision to treat that cancer first, was made.
Patient F was diagnosed in December 2021 and a 2-year treatment on chemotherapy was initiated right away.
Patient G was diagnosed in January 2022 and started chemotherapy treatments in April 2022.
Patient H was diagnosed in September 2018 and had a liver resection shortly after that.
Patient I was diagnosed in September 2023 (incidental finding) and commenced chemotherapy in October 2023.
Patient J was diagnosed in August 2017. She had a liver resection and was not offered any adjuvant therapy and did not know to ask for it.
Patient K was diagnosed in December 2021 and began chemotherapy in January 2022.
Patient L was diagnosed in December 2021 (an incidental finding) and had surgery in May 2022. No chemotherapy prior to surgery.

4. Experiences With Currently Available Treatments

The current first-line standard of care treatment is gemcitabine-cisplatin and durvalumab (gem-cis-durva), a protocol that includes an immunotherapy drug (Ramjeesingh et al., 2023). On February 3, 2023, durvalumab was approved for reimbursement for CCA to be used with gem-cis. Until recently, durvalumab was the only immunotherapy drug approved for CCA in Canada. In the summer of 2024, pembrolizumab and gem-cis were approved for first-line treatment. "The immunotherapy-plus-chemotherapy combination helped people live longer" (National Cancer Institute, 2024).

Interviewed patients' average time spent on gem-cis-durva was 9 months. All the patients received gemcitabine, and, except for one person, all patients also received cisplatin. Half of the patients (Patients A, B, C, E, I, & L) received the first-line treatment standard of care chemotherapy Gem-cis-durva protocol, and the other half had different initial treatments.

Patient D *clarified that when diagnosed,* **"I was 4 months pregnant."** *She also explained,* **"I received Carboplatin and paclitaxel weekly while I was pregnant. Once I had my daughter, I was switched to Gem-cis-durva. I also had 3 cycles of FOLFOX prior to Pemazyre."** Although she received a chemotherapy consistent with pregnancy, her protocol was changed to Gem-cis-durva after the birth of her child.

Patient F *stated that before Pemazyre, she had* **"Gemcitabine and Abraxane. They thought it was pancreatic cancer."**

Patient G *explained,* **"I was supposed to have received 4 different groups of drugs. I do not remember which ones I had first, but they include: Fluorouracil (5FU), Leucovorin, Oxaliplatin, Paclitaxel, Carboplatin, Gemcitabine and Cisplatin."**

Patient H *acknowledged,* **"I was on Gem-cis for 4 months."** Durvalumab was not an approved part of the standard of care when Patient H had her treatment.

Patient J *described,* **"I had the liver resection in 2017, radiofrequency ablation in August 2018, Gem-cis in February 2020, stereotactic body radiation therapy (SBRT) in April 2021, and SBRT again in September 2021."** Durvalumab was not an approved part of the standard of care when Patient J had her treatment.

Patient K *indicated,* **"After the 2 chemo treatments for pancreatic cancer, I was switched to Gem-cis. I was not eligible for durvalumab. I do not remember the names of the pancreatic cancer chemotherapy."**

The health-related quality of life (HRQoL) for patients is reduced while on systemic chemotherapy (Dixit et al., 2024). "The most frequently reported symptoms were fatigue, lack of appetite, difficulty sleeping, constipation and pain" (Lewandowska et al., 2020, p. 7). The patients interviewed reported other symptoms, including nausea, loss of train of thought, inability to move, hair loss, swelling of the feet, hands and face, and shortness of breath on exertion.

Patient B *described,* **"The QoL on the first chemo treatment was fine. I did well. The second time I was on the gem-cis-durva, my health declined each month. The nausea got worse. I felt like I had the flu all of the time. There was also a loss of train of thoughts."**

Patient C *stated,* **"I was tired. I didn't feel like I could plan anything in case I started feeling unwell."**

Patient D *also felt,* **"My quality of life was not better. I had nausea, loss of appetite, inability to move, and drowsy."**

Patient F *stated,* **"I thought my quality of life was good (but when I compare it to pemigatinib, it wasn't). My tummy was swollen, my legs were swollen, my feet were swollen, I lost my hair, and my face was swollen from the steroids. I had to quit work. I was always cold on chemo day and sluggish and short of breath on exertion for a few days following the chemo before improving. After the first few days following treatment, I managed to cope with the children and home."**

Patient H *explained,* **"I had fatigue, tremendous tiredness where I was physically weak, and nausea. I continued with my activities. I had less stamina. I can usually cycle for long periods but could only cycle for 1 block."**

Aspects of their treatment which were more difficult to control were:

Patient A *experienced a complication, which was a setback for her treatment. She expressed that,* **"On June 11, 2024, while having the FOLFOX treatment, my arm went 'dead'. I went to the hospital for a CT scan, although I waited a number of hours. I was admitted the following day and had an MRI. I had a cyst on the brain putting pressure on my brain to give me the symptom. I had 3 surgeries to try and get rid of the cyst. The last one was October 13, 2024. I spent 3 months in rehab for my arm and leg that went numb after my second surgery. I also got E. coli infection when they drained the fluid from my head. I have been off chemo for 5 months now. This has been the toughest part."** She has been unable to access Pemazyre due to the cost, although she was able to access the drug in mid-November with the Ontario government covering the cost.

Patient B *described*, **"The nausea got worse with each treatment and the anti-emetics were only able to take the edge off – never took it away. Flu-like symptoms were difficult to control."**

Patient C *explained,* **"The fatigue was difficult to control. I was able to control the nausea with the anti-emetic drugs. I have some ascites so am taking morphine for that discomfort."**

Patient D *identified this aspect that was difficult to control*, **"The nausea and the inability to move and drowsiness."**

Patient E *stated,* **"I felt sick in a cyclical pattern, hard to control."**

Patient G *specified,* **"I felt weak and couldn't help do anything around the house."**

Patient H *indicated*, **"I was not feeling well and deteriorating significantly. I was short of breath on exertion, couldn't climb stairs anymore and would have to have a sleep during the afternoon."**

Patient I *declared,* **"The nausea was difficult to control. The constipation was terrible. I had neuropathy prior to Chemo. Nothing helps the neuropathy."**

Patient K *indicated*, **"I was tired, short of breath, poor quality of life. Near the end of my time on chemo, I had a severe drop in my RBC, WBC and platelet counts. The decision to stop chem was made at that time."**

Patient L *detailed*, **"My quality of life on chemo was not great. I was exhausted all the time. A little bit of nausea. My platelets and WBC counts dropped."**

Only two patients, **Patient F and Patient J**, did not have aspects of the chemotherapy that were difficult to control.

Symptoms also impacted the patients' daily living activities (ADLs). Caregivers had to assume more duties around the home and with childcare. There are concerns about finances, and in one instance Patient L's spouse had to sell their side business to manage being a caregiver. The cost was part of the problem for the 3 people unable to access Pemazyre, making it unattainable for them.

***Patient G** explained,* **"My husband is worried. When I was on the chemotherapy, he was doing everything. Now that I am on Pemazyre, we share the chores together. Financially it is a burden as we are spending our savings on medications. It is getting tight." Patient G** is paying for Pemazyre out-of-pocket.

***Patient K** expressed,* **"It has been hard on my wife and my parents. Parents call me a lot and I visit them in Vancouver every 2-3 months. My wife transports me to wherever I must go, she has to do everything, she works outside the home because someone has to pay the bills. She is my everything."**

***Patient L** acknowledged,* **"My family has been impacted hugely. My sons don't really like to talk about it although I give them opening and space to talk. My husband is stressed. He holds a CFO position and had a side business – a tax consulting business, which he had to sell because it was just too much. He has had to do more work around the house and with the kids."**

FOLFOX is a second-line chemotherapy treatment usually used to treat colorectal cancer and pancreatic cancer as well as other cancers (Lamarca et al., 2021; Yetman, 2021). Patients must go to the hospital or treatment centre to receive this drug as it is given intravenously (IV). FOLFOX has debilitating side effects, not the least of which is peripheral neuropathy, (tingling sensation, burning sensation, or numbness) in the hands and feet which prevents patients from accomplishing the simplest of tasks such as buttoning their shirts. This can cause hypersensitivity to cold temperatures. Neuropathy often increases with additional chemotherapy treatment (Yetman, 2021).

Five patients were treated with FOLFOX.

***Patient A** acknowledged* **"I was on gem-cis-durva from May 2022 to February 2023 (10 months). I was on FOLFOX from February 2023 to June 2024 (17 months)."** Patient A could not access Pemazyre until Nov 14, 2024, through the Ontario government's approved case-by-case coverage.

Patient C** said, "I had 8 full cycles of Gem-cis-durva and my numbers went down. I had one cycle of durva alone and the numbers started going up, so FOLFOX was started and the numbers went down again."** She was trying to figure out how to access Pemazyre which is why she went on FOLFOX.

Patient D** stated, "…was on the Gem-cis-durva from February 2023 until March 2024 (I was off for 1 month so I could travel) and I had 3 cycles of FOLFOX from March 2024 until May 2024."**

***Patient G** commented* **that she had four therapies but did not know which order they were given. FOLFOX drugs were one of the therapies.**

Patient L** explained, "I was on capecitabine (adjuvant therapy) from August 2022 to January 2023, Gem-cis-durva April 2023 to January 2024, Durvalumab alone for February 2024 to March 2024, and FOLFOX April 2024 to July 2024."** When she describes how well the different therapies controlled the tumour, *she remarked***, "The capecitabine did not control any risk of recurrence. The Gem-cis-durva kept the tumour stable. I was never told my tumour markers. The durvalumab alone and the FOLFOX did not control the tumour. There was growth while on these last 2 therapies."** She has been without any treatment since July 2024. As of November 30, she has submitted her paperwork and is still waiting for the paperwork to be approved before she can access Pemazyre.

With cholangiocarcinoma, most people have vague symptoms to begin with, and by the time they see their physician, they already have unresectable cancer (Vogel et al., 2024). Unfortunately, when a person is diagnosed with CCA, they are usually diagnosed at an advanced stage: approximately 65% of patients have unresectable disease, and up to 50% already have metastasis at the time of diagnosis (Vogel et al., 2024).

When liver resections are recommended, they need to occur sooner rather than later. If time is allowed to progress, the cancer will spread, as shown by **Patient A**. She was diagnosed in May 2022; and received chemotherapy later that month, which lasted until February 2023. She was then scheduled for a liver transplant, but it was cancelled in May 2023 as the cancer had metastasized to her lymph nodes and her pelvis.

These patients experienced recurrences after liver resections:

Patient B *stated*, **"… I had a liver resection on August 28, 2023. After the recurrence was diagnosed, I started on gem-cis-durva again from January 30, 2024 until September 2024."**

Patient E *specified*, **"I had surgery in August 2023 to remove the tumour. The margins were not clear. I had a second surgery in November 2023, and the margins were clear following that surgery. In March 2024, I was started on Gem-cis-durva as well as radiation to the tumours in the lungs."**

Patient H *detailed*, **"...They removed 40% of my liver and found there was vascular involvement (malignant). They tried adjuvant therapy. I was sick after 1 week, so they stopped it and then tried again 1 week later. I had abdominal spasms, and I collapsed on the street, so I stopped taking the therapy."** *Later in the interview, she said*, **"After surgery, I was able to live for 3 years and 1 month without intervention."** *Then, she was* **"on Gem-cis for 4 months"** *and* **"had a few weeks of radiation."** *She was fortunate to be able to access Pemazyre through the compassionate access program and as she stated,* **"I am still on Pemazyre. I have had 35 cycles (745 days on therapy)."**

Patient J *revealed,* **"I had surgery: a liver resection in August 2017 with clear margins. I was not offered adjuvant therapy, and I didn't know to ask."** Later in the interview, she shared**, "There was a recurrence in my liver in August 2018 which I had RFA (radiofrequency ablation) which removed evidence of disease. I had another recurrence in my liver in December 2019. My doctors wanted me to have a liver transplant but I was denied in Canada and so I went to Houston and couldn't have one there either. We moved to Israel (my husband is an Israeli), because I couldn't seem to get a liver transplant or chemotherapy in Canada. I was offered chemotherapy in Israel which I started in February 2020."**

Patient L *indicated*, **"I had a liver resection (with clear margins) and removal of gall bladder in May 2022. I was on capecitabine (adjuvant therapy) from August 2022 to January 2023, Gem-cis-durva April 2023 to January 2024, Durvalumab alone for February 2024 to March 2024, and FOLFOX April 2024 to July 2024. No chemo since July 2024."** She expressed that there was a recurrence while she was on capecitabine. She was unable to access Pemazyre. As of November 30, although the appropriate paperwork has been submitted, she is still waiting for the approval from the Ontario government.

Capecitabine is another systemic chemotherapy used to treat certain types of cancers (breast, colon, rectal, stomach, esophageal and pancreatic) (WebMD, 2024). "It works by slowing or stopping the growth of cancer cells" (WebMD, 2024). Although capecitabine did not meet the primary endpoint of improving overall survival in the BTC patients, it did show overall survival rates of 24.4 months in the capecitabine group compared with 17.5 months in the observation group when used as adjuvant therapy post-surgery and is considered standard of care (Primrose et al., 2019).
Two of our interviewed patients accessed capecitabine therapy.

Patient L *explained that she had surgery in May 2022 and then started the adjuvant capecitabine therapy a few months later.,* **"…I have had capecitabine (adjuvant therapy) from August 2022 to January 2023."** She asserted that the tumour recurred even while on the adjuvant therapy, capecitabine.

Patient H *stated*, **"…They tried adjuvant therapy. I was sick after 1 week, so they stopped it and then tried again 1 week later. I had abdominal spasms, and I collapsed on the street, so I stopped taking the therapy."**

5. Improved Outcomes

The telephone / Zoom qualitative interviews served as a constructive and informative means of connecting with CCA patients to learn of their unique and oftentimes heartfelt journeys. The patients thoughtfully provided information on their disease progression and their thoughts regarding the much required improvements to help improve patient outcomes. Pemazyre is an oral medication that allows patients to live their lives without being constrained by having to go to the hospital. Oral medication also saves their veins, as chemotherapy can be extremely hard on the blood vessel walls. Pemazyre also increases their survival time. In addition, once Pemazyre is an approved targeted therapy, other second-generation FGFR2 fusion mutation drugs can be offered in Canada, starting with clinical trials when Pemazyre fails.

They all expressed concern about the aggressive nature of this cancer and were thankful to have another choice after the first-line therapy ceased to work. When asked about their experiences on Pemazyre, they felt that being able to take the drug **gave them hope** and **allowed them to live longer** compared with having nothing available after first-line chemotherapy. They also spoke about the hope for a second-generation targeted therapy drug called cancer growth inhibitor becoming available while they were on Pemazyre for use when Pemazyre ceases to work. **Patient J** has begun to seek out second-generation targeted therapies (Tinengotinib) in Europe, as her Pemazyre was stopped, and she is currently on FOLFOX.

A few statements from patients are included.

Patient A *stated,* **"It is clear that this drug is very likely going to extend my life significantly. It could buy me time for other valuable therapies to come online in the future. To have quality of life, I need to have hope. and the hope of accessing this drug keeps me going."** Patient A was able to access Pemazyre in mid-November because the Ontario government agreed to cover the expense.

Patient G *commented,* **"I want this drug to be available to everyone who needs it. There should be no cost associated with being alive."**

Patient H *acknowledged,* **"With this cancer, you are faced with terrible things. Knowing that you are going to have help covering the cost of Pemazyre is huge. It is not fair that everyone cannot access this drug. It provides a huge life enhancement."**

6. Experience With Drug Under Review

The drug Pemazyre (pemigatinib) targets the FGFR2 fusion mutation, which is almost exclusively associated with intrahepatic cholangiocarcinoma (iCCA) (Ramjeesingh et al., 2023, p. 7137; Vogel et al., 2023). Ten to fifteen percent (10-15%) of all patients who have iCCA will have the FGFR2 fusion mutation, which is the alteration that Pemazyre targets. There are companies in Canada that can test the tissue or blood of any Canadian who requires biomarker testing. Biomarker (molecular) testing is available to all Canadians, but it may have a cost and must be ordered by a physician. All patients with cancer should have molecular testing performed in a timely manner to identify any actionable mutations: FGFR2 fusion testing is required to identify eligible patients before they can receive Pemazyre (CADTH, 2022). Thankfully, in Canada, all CCA

patients can have funded access to molecular testing, and in some provinces, FGFR2 fusion testing is covered by the government.

Currently, in Canada, no targeted therapies are approved or recommended for reimbursement for CCA except in Alberta and Quebec, which cover the cost of the drug Pemazyre. Pemazyre (pemigatinib) has shown an overall response of 37% in patients in the FIGHT-202 trial (Vogel et al., 2024). No research compares life expectancy using FOLFOX and Pemazyre. The patient experience tells a different story. **Their life while on Pemazyre is "normal"**. Patients can undergo Pemazyre therapy in the comfort of their own home because it is an oral therapy – a highly sought after and much appreciated commodity. FOLFOX is given intravenously, so a trip to the cancer centre/hospital is required religiously. This is costly in time and resources to patients and their caregivers (e.g. time off work and / or school, parking fees, gas, treatment related side effects associated with IV) as well as to the health care system (e.g. staff, facility spaces, materials, and equipment) compared with an oral medication.

The patients' positive experience while undergoing the therapy should be a testament to the reaffirming and undeniable request that Pemazyre should be funded for every eligible Canadian. Of the three patients who were not on the drug when interviewed, two are now happily accessing it: as of November 30, the last patient is still waiting for approval from the Ontario government.

From the interviews, three patients stopped taking Pemazyre, and their average time on the drug was 10.5 months, ranging from 3 to 21 months. Out of the six patients remaining on the drug, they have been on Pemazyre from 2 to 26.3 months, with an average time on the drug of 12.3 months and still counting. Two patients just began their course on Pemazyre in November and are not included in this calculation.

When conversing with the patients, it became abundantly clear that responses to Pemazyre were overwhelmingly encouraging. For quality of life (QoL), patients rated their time on Pemazyre from 6 to 10, which was surely better when compared to their chemotherapy counterpart. **The average rating for quality of life on Pemazyre for the patients is 9 out of 10.** They did experience side effects, some of which included thinning of hair (***Patients B, C, D, E, F, H , J***), fingernail and toenail issues(***Patients B, E, F, H, J, K)***, watching their dietary phosphate intake and having dry eyes and longer eyelashes (***Patients B, C, D, G, J),*** and having eye doctor appointments more regularly. Despite these treatment-associated side effects, the patients interviewed emphasized that the side effects were certainly worth the benefits with respect to their quality of life while on the targeted drug.

The following are their direct quotations on how they felt about Pemazyre:

Patient B *acknowledged that she would rate her QoL on Pemazyre* **"An 8. I have amazing energy and cardio-wise, I can run up the stairs and walk uphill without any problems. I have only had one bout of unwellness which lasted only a few hours and then stopped. Even my husband has noticed the difference. My appetite is 10 out of 10."**

On November 29, Patient B contacted CHCC to relay the results of the CT scan done on November 20. **"For the first time ever, my tumours in all areas (liver, lungs, lymph nodes) have shrunk by approximately 25%. Never on chemo did my tumors shrink. So, this is definitely positive."**

Patient C *asserted,* **"It was a 10. I felt normal. Fatigue was gone. People couldn't tell that I had cancer."**

Patient D *acknowledged that she would rate the drug a* **"10. I felt normal. I had more energy. We were able to go for walks, have dinners out."**

Patient E *said out of 10, she would rate being on Pemazyre* **"Presently a 7. For the first 3 cycles, I felt great, and I had energy, and it would have been a 10. Then I had a surprise surgery as my bowel got pinched in a hernia in my diaphragm. That surgery was in August 2024. Since that surgery, I am still recovering. I have chronic pain which is worse in the evening."**

Patient F *is thrilled and rated Pemazyre a* **"10. I love Pemigatinib. I feel normal, have so much energy, and have returned to work (I love my job). My tumors shrunk for the first 3 months, and now they are stable."**

Patient G *had a more complex experience with Pemazyre.* **"9. When I first went on Pemazyre, I took the full dose as prescribed. In January 2024, my joints in my back and legs were so sore I couldn't walk. My eyes were also really dry. We suspended the treatment for 5 weeks. During those 5 weeks, I took steroids, went to physio, and had acupuncture. I went back on Pemazyre at a lower dose and take the drug for one week, and then go off for one week. I feel great. I have more energy. I am walking 3 km/day. I still get tired, but I can do things like I did before. I help my husband do chores, cooking, cleaning and laundry around the house now."**

Patient H *rated Pemazyre a* **"10. This drug was an energy restorer. I felt normal again. No longer needed to sleep during the day. I even took up pickleball." *She*** *then explained,* **"My mother was ill, and it allowed me to look after her until she died a year ago. She was upset when I was diagnosed because children are not supposed to die before their parents. This drug allowed me to spend time with her and help her through her last years of life."**

Patient J *remarked,* **"I would give it a 6 or 7. We played around with the dose. I was on the low dose most of the time. I was living an active life. I was still working. Every day was a bit different depending on where I was in the cycle. I was doing my best to live a normal life even though I had symptoms."**

Patient K *would rate his QoL on Pemazyre,* **"An 8. Sometimes I am tired and have some ocular issues, (I do see the eye doctor every 6 weeks). My energy levels are good, and my appetite is good."**

7. Anything Else?

Direct patient input through semi-structured qualitative telephone and Zoom interviews provided a comprehensive understanding of the cholangiocarcinoma and treatment experience from the patient's perspective. The patients were emphatic about why Pemazyre should be added as a targeted therapy for patients with the FGFR2 fusion mutation. These comments are critically important in the patient's cholangiocarcinoma journey. As stated previously, Patients B, C D, F, H, all called Pemazyre an energy restorer. They had so much energy compared to being on chemotherapy. They could make plans as this drug allowed them to go about their lives normally. Even though **Patients B, C, D, E, F, G, H, J and K** all had symptoms (as previously noted), they still would rather be on the drug than not. **Patients A and I** just received approval in November and are happy to be going on the drug as it will extend their lives, however long. **Patient L** is waiting for the paperwork to go through. ***Patient A*** expressed the sentiment well: **"It is clear that this drug is very likely going to extend my life significantly. It could buy me time for other valuable therapies to come online in the future. To have quality of life, I need to have hope. and the hope of accessing this drug keeps me going."**

Patients across Canada can access a precision oncology lab in Canada. Provinces could come together with inter-provincial agreements to cover the cost of patients so all patients may be tested. As Canada supports more targeted therapies, the strain on the healthcare system may be reduced, as targeted drugs, oral medications, can be taken at home. The health care burden will ultimately drop, and the financial burden of

the disease will improve. Patients can return to contributing to their communities either in volunteer form or back to work, as demonstrated by ***Patient F,*** *who commented*, **"I got to go back to work. I love my job!" But more importantly, patients will resume some former sense of normalcy as they begin to take care of their families, assume household chores, take care of aging parents, young children as they return to a glimpse of their former selves.**

This is the first targeted therapy approved by Health Canada for cholangiocarcinoma, and patients want something else besides systemic infusional chemotherapy to treat this rare and aggressive cancer. Using effective, easily administered and less toxic targeted therapeutics is of paramount importance. Instead of affecting all the cells of the body, Pemazyre targets the cells that have the FGFR2 fusion mutation. The drug demonstrated a **median overall survival of 17.5 months, more than twice what was expected** (Vogel et al., 2024). Some patients have been alive and living well on the drug for over two years. Equally important is that there are second- and third-generation drugs that target this mutation, and they are available in clinical trials in other countries. However, none of these trials can ever come to Canada because the availability of Pemazyre (pemigatinib) as the standard of care and the failure of Pemazyre is a requirement for the second or third generation clinical trial enrolment. Clinical trials bring innovation and financial support to the province supporting them.

Everyone should have biomarker testing done early in their treatment journey. This is so patients can start planning for second-line treatments (hopefully targeted therapies) before their first-line treatment ceases to be effective (Ramjeesingh et al., 2023). ***Patient F*** *asserted,* **"There are no other options. Everybody that needs this drug should receive it. Everyone should be treated for biomarkers when they are diagnosed, or at least at the beginning of their cancer treatments."**

The five-year survival rate is low for CCA, and according to the Canadian Medical Association Journal (CMAJ), the age-standardized mortality rate per 100,000 is rising for hepatocellular and cholangiocarcinoma (Brenner et al., 2024). All the other cancers are stabilizing or decreasing. Canada is lagging behind other developed countries for the targeted therapies available for cholangiocarcinoma. All the patients who were interviewed felt that Pemazyre should be affordable and accessible to all patients who have the FGFR2 fusion mutation. Patients should not be denied the chance to live; this has to change for CCA patients. ***Patient J*** *sums it up by stating Pemazyre gives people*: **"The Hope. It buys time until more treatments and therapies can come out or be discovered and offered."**

Incorporating Pemazyre as a second-line treatment, albeit first-line targeted therapy, addresses an unmet need for the cholangiocarcinoma population: providing hope, prolonging life, and maintaining or improving overall QoL when compared with QoL on chemotherapy. As a collective group, we strongly support and urge a positive funding recommendation for reimbursement be issued for Pemazyre as a targeted therapy in second-line treatment following the standard of care systemic chemotherapy, gem-cis plus immunotherapy (durvalumab or pembrolizumab), for the treatment of cholangiocarcinoma. We believe that adding this oral medication enhances the patient's life by giving them hope for the future, improving their quality of life and increasing their overall length of survival.

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH reimbursement review process, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

   No

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

   No

3. List any companies or organizations that have provided your group with financial payment over the past 2 years AND who may have direct or indirect interest in the drug under review.

Table 2: Financial Disclosures

Check Appropriate Dollar Range With an X. Add additional rows if necessary.

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Incyte		X		

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: **Brenda Clayton**
Position: **President & CEO**
Patient Group: **Cholangio-Hepatocellular Carcinoma Canada**
Date: **December 11, 2024**

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Appendix B: Flyer

ARE YOU A LOCALLY ADVANCED OR METASTATIC BILIARY TRACT CANCER PATIENT WHO HAS RECEIVED OR IS RECEIVING PEMAZYRE (Pemigatinib)?

IF SO, WE *REALLY NEED YOUR HELP!*

Pemazyre (pemigatinib) is currently under a funding review in Canada for the treatment of locally advanced unresectable or metastatic (stage IV) biliary tract cancer.

Cholangio-Hepatocellular Carcinoma Canada (CHCC) is leading a patient evidence re-submission for this first line targeted treatment of adult patients diagnosed with locally advanced unresectable or metastatic biliary tract cancer and who have the FGFR2 fusion mutation (biomarker).

We are looking for biliary tract cancer patients (or their caregivers) with firsthand experience with this therapy, who are willing to share their valuable story via phone or Zoom. The patient's perspective will help to inform our patient input submission and provide the expert committees in Canada with this important insight as they prepare to issue their funding recommendation for this drug in Canada.

The patients (or caregivers) who participate in the interview process will have their privacy and confidentiality respected and always maintained. Their input will be completely anonymized in the submission. The telephone interview will last approximately 60 minutes and while there is no guarantee, it may help to get this drug funded throughout Canada.

Patients and caregivers may consent to have their contact information (name, phone # and email address) sent to Brenda Clayton, and, in turn, the patient/caregiver will be contacted with an appointment time and date for participation in the telephone interview.

Alternatively, the patient/caregiver may contact Brenda directly ASAP to advise of their willingness to participate in a telephone or Zoom interview to help form the patient input submission to make a meaningful impact:

Brenda Clayton, [redacted]; local: 403-701-7017 or toll free: 1-877-694-0314

Please contact Brenda ASAP to schedule the phone interview.

Thank you for making a difference in the lives of biliary tract cancer patients and their families!

We look forward to hearing from you.

Appendix C: Patient Interview Data

PEMIGATINIB(PEMAZYRE) SUBMISSION: CHOLANGIOCARCINOMA

PATIENT INTERVIEW DATA

PART A: DEMOGRAPHIC INFORMATION

INTERVIEW QUESTION	RESPONDENT A: PATIENT	RESPONDENT B: PATIENT	RESPONDENT C: PATIENT	RESPONDENT D: PATIENT	RESPONDENT E: PATIENT	RESPONDENT F: PATIENT	RESPONDENT G: PATIENT	RESPONDENT H: PATIENT	RESPONDENT I: PATIENT	RESPONDENT J: PATIENT	RESPONDENT K: PATIENT	RESPONDENT L: PATIENT
1. INTERVIEW DATE, TIME AND METHOD (TELEPHONE, EMAIL...)	October 26, 2024 4:00-5:00 p.m. Telephone	October 24, 2024 3:00-4:00 p.m. Telephone	October 26, 2024 3:00-4:00 p.m. Telephone	October 28, 2024 9:15-10:15 a.m. Telephone At the time of the interview, the patient has been in hospital for 2 days because of increasing heart rate.	October 28, 2024 3:00-4:00 p.m. Telephone	October 31, 2024 9:00-10:00 a.m. Telephone	October 31, 2024 12:00-1:00 p.m. Zoom	November 1, 2024 8:30-9:30 a.m. Telephone	November 2, 2024 8:00-9:00 a.m. Telephone	November 2, 2024 12:00-1:00 p.m. Zoom	November 7, 2024 10:00-11:00 a.m. Telephone	November 7, 2024 12:00-1:00 p.m. Telephone
2. PATIENT'S CURRENT AGE, AGE AT THE TIME OF DIAGNOSIS, GENDER (M,F,NON-BINARY)	Female 62 years old 59 years old at diagnoisis	Female 56 years old 54 years old at diagnosis	Female 46 years old 44 years old at diagnosis	Female 26 years old 24 years old at diagnosis	Female 50 years old 48 years old at diagnosis	Female 43 yrs old 40 years old at diagnosis	Female 76 years old 74 years old at diagnosis	Female 68 years old 62 years old at diagnosis	Female 79 years old 78 years old at diagnosis	Female 38 years old 31 years old at diagnosis	Male 57 years old 55 years old at diagnosis	Female 45 years old 42 years old at diagnosis

3. TREATMENT PROTOCOL	Gem-Cis-Durva	Chemotherapy followed by liver resection, back on chemotherapy, followed by Pemazyre	Gem-Cis-Durva	Carboplatin and paclitaxel while pregnant and then Gem-Cis-Durva	"I had a resection first." "When treatment protocol happened, it was Gem-Cis-Durva."	Gemcitabine-Abraxane plus naturopathic treatments "It was thought to be pancreatic cancer initially."	"From April 2022 until June 2023, I had four different therapies: Fluorouracil (5FU), Leucovorin, Oxaliplatin, Paclitaxel, Carboplatin, Gemcitabine, and Cisplatin. I do not remember the combinations, but there were four different groups."	Gem-Cis	Gem-Cis-Durva	Liver resection, SBRT, Gem-Cis, Durvalumab	Chemo for pancreatic cancer initially for 2 cycles, then switched to Gem-cis after that as it was determined to be cholangiocarcinoma	"I had a liver resection (with clear margins) and removal of gall bladder in May 2022. I was on capecitabine (adjuvant therapy) from August 2022 to January 2023, Gem-cis-durva April 2023 to January 2024, Durvalumab alone for February 2024 to March 2024, and FOLFOX April 2024 to July 2024. No chemo since July 2024."
4. CITY, PROVINCE OR STATE, COUNTRY	Newmarket, Ontario, Canada	High River, Alberta, Canada	Kelowna, British Columbia, Canada	Kitchener, Ontario, Canada	Stettler, Alberta, Canada	Blackie, Alberta, Canada	Mississauga, Ontario, Canada	Toronto, Ontario, Canada	Barrie, Ontario, Canada	"I was living in Edmonton, Alberta and moved to Israel in 2020 so that I could get treatment that Canada did not offer."	Vernon, British Columbia, Canada	Grimsby, Ontario, Canada
5. A. MARITAL STATUS (S,M,D)	Single	Married	Married	Married	Married	Married	Married	Married	Married	Married	Married	Married
B. CHILDREN	N/A	N/A	N/A	1 daughter	2 daughters	5 children ages 5-14	2	2	"I have 2 children a son and daughter."	1	2 stepdaughters	2 children
C. GRANDCHILDREN	N/A	N/A	N/A	N/A	3	N/A	3	1	"I have 4, but one died of sarcoma 9 years ago at age 27 years."	N/A	1 step grandson	N/A
6. OUTREACH METHOD? **A. CANADIAN CLINICIAN** **B. OTHER**	Medical oncologist	"I have only seen a Canadian clinician."	"Canadian clinician, although I have hired a company to put our files together so I can approach Princess Margaret Hospital (Ontario) or the USA possibly."	Canadian clinician. Has not reached out to the USA yet.	Canadian clinician. Has not reached out to the USA yet.	Canadian clinicians at this time.	Canadian clinician	Canadian clinician	"I have only used Canadian clinicians so far".	Canadian clinician and moved to Israel.	Canadian clinician	Canadian Clinician
7. TREATMENT CENTRE	**Stronach Cancer Centre** Newmarket, ON	**Tom Baker Cancer Centre** Calgary, AB	**Royal Inland Hospital** Kamloops, BC	**Grand River Regional Cancer Centre** Kitchener, ON	**Central Alberta Cancer Centre** Red Deer, AB	**High River Community Cancer Centre** High River, AB **Tom Baker Cancer Centre** for appointments with medical oncologist only	**Credit Valley Hospital** Mississauga, ON	**Princess Margaret Cancer Centre** Toronto, ON	"I go to Royal Victoria Regional Health Centre in Barrie."	"I had surgery at the U of A. I now go to the Rabin Medical Centre."	**Jubilee Hospital Cancer Centre** Vernon, BC	**Juravinski Cancer Centre** Hamilton, ON

PART B: DISEASE EXPERIENCE/EXPERIENCE WITH CURRENTLY AVAILABLE THERAPIES

INTERVIEW QUESTION	RESPONDENT A: PATIENT	RESPONDENT B: PATIENT	RESPONDENT C: PATIENT	RESPONDENT D: PATIENT	RESPONDENT E: PATIENT	RESPONDENT F: PATIENT	RESPONDENT G: PATIENT	RESPONDENT H: PATIENT	RESPONDENT I: PATIENT	RESPONDENT J: PATIENT	RESPONDENT K: PATIENT	RESPONDENT L: PATIENT
8. YOUR BILIARY TRACT JOURNEY. **A. WHEN WERE YOU FIRST DIAGNOSED WITH BILIARY TRACT CANCER?**	May 6, 2022	January 24, 2023	November 9, 2022	October 12, 2022	April, 2023	December, 2021	January, 2022	September, 2018	"In September 2023, I fell down some stairs and fractured my collarbone. When I went to the hospital, it was picked up on the x-rays I had."	August, 2017	Early December, 2021	December, 2021
B. WERE YOU SYMPTOMATIC, WHICH LED TO INVESTIGATIONS? TELL ME A BIT ABOUT IT.	"In April 2022, I was experiencing stomach pains so bad that I went to the walk-in clinic in Newmarket. I had an ultrasound (U/S) immediately. They saw a mass and did a biopsy immediately. I also had blood work done."	"Extremely exhausted and had been for about a year – thought it was just getting older. Had trouble walking up hill – out of breath (thought I had a cardiac issue). Three months before I saw my doctor, I had a chest cold that I couldn't shake. When getting into the car, I experienced pain in my upper right abdomen a couple of times (seemed to depend on how much I twisted). That was in December 2022."	"I was tired, had a significant bulge in my sternum. Went to the doctor in October 2022. Had blood work, CT scan and an ultrasound guided biopsy."	"I was 4 months pregnant. In September I had a sharp, stabbing pain on my right side. I went to the ER, and they did an Ultrasound and some blood work. The ultrasound showed lesions (they weren't sure if they were infections, cancer…) A biopsy was done on October 4, 2022."	"I had weird, strange back pain that would come and go. I also had some indigestion. I went to see the doctor about it. I had an ultrasound in March 2023, which showed a 5cm mass in my liver."	"Two years prior to my diagnosis, I had a rash on my hands that wouldn't go away. I also developed some food sensitivities and so altered my diet to exclude (gluten, sugar and lactose). Food allergies run in my family, so I thought I was starting to develop them. I had random GI issues, like bloating and diarrhea. I had a stomach-ache which was high up under my ribs. It was hard to touch and hurt. After 1 week, I went to the urgent care facility. They did a physical exam and blood work. My liver enzymes were elevated. I had an ultrasound the next day and then saw the doctor the day after that where it was confirmed that I had stage IV cancer, primary unknown. She looked at my symptoms and wanted to do a colonoscopy, but I would have to wait 6 months, so I was booked for a biopsy of my liver. The biopsy said it could be cervical cancer, pancreatic cancer or	"I had a really bad stomach-ache. My husband took me to the doctor; he thought it was gall stones. Had an ultrasound and there were no stones but a cyst on the liver was noted. I was then referred to an internist who said a lot of people had cysts. I had a biopsy of the cyst in January 2022 and came back cancer. I was then referred to a medical oncologist."	"I had a random abdominal ultrasound in August 2017. I had ultrasounds every 6 months. I had weight loss but no other symptoms. A radiologist who read my ultrasound in August 2018 felt I should see another doctor, so I was sent to Sunnybrook, but then my care was transferred to Princess Margaret Hospital. They did a work-up, CT scan, and biopsy and then said we think you should have surgery. They removed 40% of my liver and found there was vascular involvement (malignant). They tried adjuvant therapy. I was sick after 1 week, so they stopped it and then tried again 1 week later. I had abdominal spasms, and I collapsed on the street, so I stopped taking the therapy."	"I was asymptomatic. It was the broken collarbone that brought me to hospital."	"I had yearly PET scans since I was diagnosed with Wilson's disease in 2005. My liver is cirrhotic. I was asymptomatic. The scan picked up a 2cm tumour and my CA19-9 was high."	"I had a bulge over my stomach, lots of inflammation and I was nauseated when I ate."	"I was having gall bladder issues, which was pain after eating. The tumour was an incidental finding on an ultrasound. It was biopsied In January 2022 and received the results in February 2022. I had surgery in May 2022."

						cholangiocarcinoma. I had tumours on my liver and in my lungs. They decided to treat me for pancreatic cancer."						
C. HOW WAS YOUR BILIARY TRACT CANCER DETECTED OR DIAGNOSED?	"Through an ultrasound (U/S), and blood work and biopsy." "GP said I needed to see a specialist right away. The doctor called the next morning with an appointment the following Thursday in April 2022."	"I had blood work in the 1st week of January 2023, spoke with the doctor about results the following week. My AST value was slightly elevated at 64. Had an ultrasound on January 20, 2023." "Diagnosed on January 24, 2023" "The ultrasound showed an 11.4cm tumor in my right lobe with solid satellite tumors throughout. The left lobe was clear."	"Through the biopsy."	"It was detected with the ultrasound and the biopsy."	"I had a biopsy in June 2023 for suspected cholangiocarcinoma."	"Diagnosed with the ultrasound, blood work and biopsy."	"By a biopsy."	"Ultrasounds, CT scan and biopsy."	"I had a CT scan, MRI, and bloodwork. I had a biopsy of my liver on October 6, 2023, and a biopsy of my lymph nodes on October 18, 2023.	"I had surgery: a liver resection in August 2017 with clear margins. I was not offered adjuvant therapy, and I didn't know to ask."	"I had an ultrasound which showed 2 big tumours in my liver (8cm and 4cm) as well as lots of lesions."	"It was an incidental finding. I was having gall bladder issues and had a scan and ultrasound, and the tumour was spotted at that time."

D. HAVE YOU EVER BEEN DIAGNOSED WITH A RECURRENCE?	"No, it has never gone away."	"Yes."	"It has never gone away."	"It has never gone away."	"Yes. In June 2024, on the MRI, there was a small tumour at the resection site and satellite tumours on the Left side of the liver."	"It has never gone away."	"It has never gone away."	"Yes."	"It has never gone away".	"There was a recurrence in my liver in August 2018 which I had RFA (radiofrequency ablation) which removed evidence of disease. I had another recurrence in my liver in December 2019. My doctors wanted me to have a liver transplant but I was denied in Canada and so I went to Houston and couldn't have one there either. We moved to Israel (my husband is an Israeli), because I couldn't seem to get a liver transplant or chemotherapy in Canada. I was offered chemotherapy in Israel which I started in February 2020."	"It has never gone away".	"Yes."
E. HAS THERE BEEN A METASTATIC DIAGNOSIS? IF SO, WHAT WAS THE DATE OF THE METASTATIC DIAGNOSIS?	"I was supposed to have a liver resection but two weeks before, they discovered a tumor in the pelvis and in the lymph node, so my surgery was cancelled. May 2023- found tumor cells in my lymph nodes. In October 2023 I had a lesion in my pelvis and then in August 2024, there was a lesion in my humerus which had radiation."	"In December 2023, diagnosed with recurrence following surgery in August 2023."	"November 9 when I was diagnosed with CCA, there were small nodules in my lungs."	"The tumors were contained within the liver. I was diagnosed with stage IV initially. I was supposed to have a liver transplant as the tumors were contained within the liver. However, I took a month off of treatment and went back to Saudi Arabia in October and when I came back, I went back on the Gem-cis-durva. I had a PET scan at that time, and it showed that the cancer had spread to my lymph nodes., so liver transplant was off the table."	"I am an unusual case. There was a small tumor in my lung and a few spots on my diaphragm. The spots on the diaphragm were biopsied and came back as mesothelioma. The tumor in the lung was then biopsied and found to be non-small cell adenocarcinoma. So, I have 3 cancers."	"On the date of diagnosis December 2021."	"I started with one tumour in the liver. There are 2 now. No other metastasis anywhere else."	"My numbers started to increase in January 2020, but it didn't show up until November 2021."	"It was in 2 of my lymph nodes initially and at the top of my liver. The date was September 2023."	"Yes."	"I had a PET scan in Kelowna in late December which showed spots in my lungs."	"In January 2023, they did a scan and the cancer had recurred."
F. LOCATION OF THE METASTATIC LESION?	"Lymph nodes and pelvis."	"It was in the remaining lobe of my liver, a couple of lymph nodes in my abdomen and many	"Lungs."	"Liver, initially."	"Liver."	"Liver and lungs."	"Liver."	"It appeared in one of my lymph nodes."	"It is on 2 lymph nodes and another spot on my liver."	"In September 2021, there were tumours in my liver and lungs. In April 2024, there were tumours in my liver, lymph nodes,	"I have lesions in my liver and lungs."	"It is on my peritoneum."

		small tumours in both of my lungs."								lungs and peritoneum."		
9. A. WHAT THERAPIES DID YOU RECEIVE BEFORE PEMAZYRE? GEM-CIS-DURVA? GEM-CIS-PEMBRO?	"While on gem-cis-durva, I felt good and was doing everything. People said I didn't look sick. I was on gem-cis-durva from May 2022 to February 2023. Then, I was on FOLFOX from February 2023 to June 2024."	"Gem-cis-durva."	"Gem-cis-durva."	"I received Carboplatin and paclitaxel weekly while I was pregnant. Once I had my daughter, I was switched to Gem-cis-durva. I also had 3 cycles of FOLFOX prior to Pemazyre."	"I had surgery in August 2023 to remove the tumour. The margins were not clear. I had a second surgery in November 2023, and the margins were clear following that surgery. In March 2024, I was started on Gem-cis-durva as well as radiation to the tumours in the lungs."	"Gemcitabine and Abraxane. They thought it was pancreatic cancer."	"I was supposed to have received 4 different groups of drugs. I do not remember which ones I had first, but they include: Fluorouracil (5FU), Leucovorin, Oxaliplatin, Paclitaxel, Carboplatin, Gemcitabine and Cisplatin."	"Surgery-liver resection." "Gem-cis, no durva." "Radiation therapy was tried as well."	"I haven't been on Pemazyre yet. Haven't been able to access it yet. I had Gem-Cis-Durva, radiation treatment and Durvalumab only once the Gem-cis was stopped."	"I had the liver resection in 2017, radiofrequency ablation in August 2018, Gem-cis in February 2020, stereotactic body radiation therapy (SBRT) in April 2021, and SBRT again in September 2021."	"After the 2 chemo treatments for pancreatic cancer, I was switched to Gem-cis. I was not eligible for durvalumab. I do not remember the names of the pancreatic cancer chemotherapy."	"I haven't received Pemazyre yet, but I have had capecitabine (adjuvant therapy) from August 2022 to January 2023, Gem-cis-durva April 2023 to January 2024, Durvalumab alone for February to March 2024, and FOLFOX April 2024 to July 2024."
B. DID THOSE TREATMENTS CONTROL YOUR BILIARY TRACT CANCER? YES/NO. PLEASE EXPLAIN.	"They helped. As I mentioned, I was feeling good. The gem-cis-durva was stopped because my doctor felt I had been on it long enough. I started FOLFOX after gem-cis-durva was stopped."	"They kept the cancer stable. No shrinkage of the tumors. I was on gem-cis-durva twice. The first time was from March 10 until July 28, 2023. I had a liver resection on August 28, 2023. After the recurrence was diagnosed, I started on gem-cis-durva again from January 30, 2024 until September 2024."	"I had 8 full cycles of Gem-cis-durva and my numbers went down. I had one cycle of durva alone and the numbers started going up, so FOLFOX was started and the numbers went down again."	"Yes, the treatments did control the cancer. My numbers were dropping, and on ultrasound, the tumour was shrinking."	"Yes. The CT scan showed that the chemo and radiation stabilized the cancer."	"Yes. There was shrinkage of the tumours. The largest tumour had shrinkage of 50%, and there was shrinkage of the other tumours in my liver and lungs for the first year. From 12-18 months, the tumours were stable, and from 18-24 months, there was some growth."	"The first 2 groups did not work, and the size increased. The third one I was on stopped the growth of the tumour, for awhile and I felt better. I got really sick on the 4th treatment and had an allergic reaction to one of the drugs. I believe it was Oxaliplatin. I had to come off of the drug. That was June 2023."	"They kept the tumour stable."	"Yes. The treatments seemed to control the main tumour in the liver. The lymph nodes have shown some growth."	"The liver resection removed the tumour. The radiofrequency ablation removed evidence of any disease. The Gem-cis was keeping the tumours under control until July 2020 and then I went off the cisplatin as my veins were shot.	"The chemo partly controlled my cancer. It stabilized it and there was some shrinkage but not as much as the doctors thought would happen."	"Yes and no. The capecitabine did not control any risk of recurrence. The Gem-cis-durva kept the tumour stable. I was never told my tumour markers. The durvalumab alone and the FOLFOX did not control the tumour. There was growth while on these last 2 therapies."

C. PLEASE DESCRIBE YOUR QUALITY OF LIFE ON THOSE PREVIOUS TREATMENTS.	"I felt good. I remained working and caring for my mother. My arms felt like a pin cushion. They were black and blue. I felt tired in December 2022. My mother died in November 2022, so that could have been the contributing factor."	"The QoL on the first chemo treatment was fine. I did well. The second time I was on the gem-cis-durva, my health declined each month. The nausea got worse. I felt like I had the flu all of the time. There was also a loss of train of thoughts."	"I was tired. I didn't feel like I could plan anything in case I started feeling unwell."	"My quality of life was not better. I had nausea, loss of appetite, inability to move, and drowsy."	"I was sick in spurts. I would have diarrhea, nausea and vomiting and then have to go to the hospital, then go off treatment and then start again."	"I thought my quality of life was good (but when I compare it to pemigatinib, it wasn't). My tummy was swollen, my legs were swollen, my feet were swollen, I lost my hair, and my face was swollen from the steroids. I had to quit work. I was always cold on chemo day and sluggish and short of breath on exertion for a few days following the chemo before improving. After the first few days following treatment, I managed to cope with the children and home."	"I was weak and laid around all day after my treatments. Although I felt better on the 3rd round of chemo drugs, I was still weak."	"I had fatigue, tremendous tiredness where I was physically weak, and nausea. I continued with my activities. I had less stamina. I can usually cycle for long periods but could only cycle for 1 block."	"I was pretty sick on chemotherapy. I was tired, nauseated, constipated and had neuropathy (which I did have before)." "I tried a couple of medications to control the nausea which helped."	"I worked full-time. I was okay. I had some nausea."	"My quality of life was not good. I was tired, had shortness of breath, nausea, difficulty walking, limbs would go numb, and I had inflammation and discomfort."	"My quality of life on chemo was not great. I was exhausted all the time. A little bit of nausea. My platelets and WBC counts dropped."
D. HOW LONG DID IT TAKE BEFORE YOU PROGRESSED ON EACH OF THOSE PREVIOUS THERAPIES?	"I was on gem-cis-durva from May 2022 to February 2023 (10 months). I was on FOLFOX from February 2023 to June 2024 (17 months)."	"The first time I was on chemo, March to July, and then liver resection. The second time, January to September 2024. My kidneys and bone marrow were starting to be affected. I stopped the chem for good in September 2024."	"I was on Gem-cis-durva from December 2022 to June 2023 (8 full cycles), Durvalumab for 1 cycle and then started FOLFOX in July until October 2023 (4 months). I had to figure out how to access Pemazyre, which is why I started FOLFOX."	"I was on carboplatin and paclitexal from October 2022 until February 2023 when I delivered my daughter. I was on the Gem-cis-durva from February 2023 until March 2024 (I was off for 1 month so I could travel) and I had 3 cycles of FOLFOX from March 2024 until May 2024."	"I was only on Gem-cis-durva for 4 cycles. The doctor took me off so they could focus on the cholangiocarcinoma before other cancer treatments."	"I was on Gemcitabine-Abraxane for 24 months."	"I don't know the time between each group of chemotherapy drugs, but I was on them for a total 14 months, from April 2022 to June 2023, with a break in January 2024 for 5 weeks."	"After surgery, I was able to live for 3 years and 1 month without intervention (September 2018 to November 2021)." "I was on Gem-cis for 4 months (January to April 2022)." "I had a few weeks of radiation (April to July 2022)."	"I was on Gem-cis-durva from October 2023 until March 2024, when I went on Durvalumab only and am still on the immunotherapy. I had 5 bouts of radiation in May 2024."	"I was on Gem-cis for 4 months, and then it stopped working, so it went from February 2020 to July 2020. I don't remember what happened from July 2020 until April 2021, except that it was COVID. I had SBRT in April 2021 and again in September 2021. I had a baby in 2021."	"I was on Gem-cis from January 2022 to December 2022. Then I was placed on pemigatinib. The tumours had some shrinkage and stabilized"	"I was on capecitabine (adjuvant therapy) for 6 months; I was on Gem-cis-durva for 10 months; I was on durvalumab alone for 2 months and FOLFOX for 4 months."

10. WERE THERE ANY PARTICULAR ASPECTS OF THE DISEASE THAT WAS DIFFICULT TO CONTROL WHILE ON THOSE TREATMENTS OR IN GENERAL?	"I was supposed to go for a liver transplant but 2 weeks prior, they discovered a tumor in my pelvis and 1 in my lymph node, so surgery was cancelled. I had radiation on the pelvic tumor in October 2023 which got rid of it. I couldn't have radiation on the lymph node because of its' location." "On June 11, 2024, while having the FOLFOX treatment, my arm went 'dead'. I went to the hospital for a CT scan, although I waited a number of hours. I was admitted the following day and had an MRI. I had a cyst on the brain putting pressure on my brain to give me the symptom. I had 3 surgeries to try and get rid of the cyst. The last one was October 13, 2024. I spent 3 months in rehab for my arm and leg that went numb after my second surgery. I also got E. coli infection when they drained the fluid from my head. I have been off chemo for 5 months now. This has been the toughest part."	"The nausea got worse with each treatment and the anti-emetics were only able to take the edge off – never took it away. Flu-like symptoms were difficult to control."	"The fatigue was difficult to control. I was able to control the nausea with the anti-emetic drugs. I have some ascites so am taking morphine for that discomfort."	"The nausea and the inability to move and drowsiness."	"I felt sick in a cyclical pattern, hard to control."	"Not really. I had some digestion problem, was put on pantoprazole and pancrelipase (creon) which helped. I don't take them anymore."	"I felt weak and couldn't help do anything around the house."	"I was not feeling well and deteriorating significantly. I was short of breath on exertion, couldn't climb stairs anymore and would have to have a sleep during the afternoon."	"The nausea was difficult to control. The constipation was terrible. I had neuropathy prior to Chemo. Nothing helps the neuropathy."	"Not really."	"I was tired, short of breath, poor quality of life. Near the end of my time on chemo, I had a severe drop in my RBC, WBC and platelet counts. The decision to stop chem was made at that time."	"My exhaustion and platelet and WBC counts."

PART C: EXPERIENCE WITH PEMAZYRE FOLLOWING CHEMOTHERAPY

INTERVIEW QUESTION	RESPONDENT A: PATIENT	RESPONDENT B: PATIENT	RESPONDENT C: PATIENT	RESPONDENT D: PATIENT	RESPONDENT E: PATIENT	RESPONDENT F: PATIENT	RESPONDENT G: PATIENT	RESPONDENT H: PATIENT	RESPONDENT I: PATIENT	RESPONDENT J: PATIENT	RESPONDENT K: PATIENT	RESPONDENT L: PATIENT
11. A. WAS YOUR BILIARY TRACT CANCER TESTED FOR ANY GENETIC OR MOLECULAR MUTATIONS? IF SO, AT WHAT POINT IN YOUR CANCER JOURNEY, AND WHAT WERE THOSE MUTATIONS IF ANY?	"Foundation One tested my biopsy, but not right away."	"Yes. I had the tumor biopsy taken in February 2023, tested in June 2023. The mutation came back FGFR2 fusion mutation. The tumor was only tested for 16 mutations. I have since asked them to retest for all of the mutations."	"In June 2023, my biopsy was tested."	"It was tested right away from the biopsy. I had the FGFR2 fusion mutation."	"It was biopsied in June 2023. I have a FGFR2 fusion mutation and RAD51C."	"The biopsy taken in December 2021 was tested in March 2022 for biomarkers. The only mutation was FGFR2 fusion mutation."	"Yes. The biopsy that was taken in January 2022 was tested in October 2022. The only mutation was FGFR2 fusion mutation."	"Yes. The biopsy was tested in the summer of 2022. I have FGFR2 fusion and IDH1 mutations."	"Yes, it was tested in October 2023. The mutation was FGFR2 fusion. My biopsy has been sent off again to see if there are any other mutations. It was sent away at the beginning of October 2024."	"It was tested in January 2020. It showed FGFR2 fusion mutation, MS stable, DAP1 and MCL1 amplification: it was retested in December 2023, and besides FGFR2 fusion, it showed ARIDIA."	"Yes. It was tested in July/August 2022. I was enrolled in the POG program (personalized onco-genomics) program. My biopsy was tested for biomarkers through the POG program. The only mutation I have is FGFR2 fusion mutation."	"Yes. The initial biopsy came back with no identifiable biomarkers. The tumour was biopsied again in September 2024 and came back with FGFR2 fusion mutation."
B. IF YOU DID HAVE TO UNDERGO TESTING, DID YOU PAY OUT OF POCKET FOR THAT TESTING?	"No. It was paid for."	"OncoHelix did the testing, and I did not have to pay for it."	"I did not pay for the testing. Incyte did."	"Yes, I had to pay out of pocket. Foundation One did the test."	"Yes, I paid out of pocket. Foundation One did the testing."	"No. PanCan (pancreatic cancer organization paid for the testing.) My husband found this organization."	"Ontario paid for the testing."	"Ontario paid for the testing."	"I did not pay for testing."	"We paid out-of-pocket for the test from Foundation One."	"No. The POG program paid for the testing."	"The testing was done through OncoHelix and C3 paid for it."
C. HOW DID YOU BECOME AWARE OF PEMAZYRE?	"My oncologist, Cholangiocarcinoma Foundation (USA) and a Canadian advocate."	"In May 2023 from my medical oncologist."	"My GP found out about the drug and let my oncologist know. It took some time before we figured out how to pay for it."	"My doctor told me about it."	"Through my own reading and the Cholangiocarcinoma Foundation in the USA."	"My medical oncologist."	"My medical oncologist."	"My medical oncologist."	"My medical oncologist told me about it. Plus, I spoke with someone from Incyte."	"My medical oncologist".	"I became aware of Pemazyre through the POG program and my medical oncologist."	"Through the cholangiocarcinoma community."
D. WERE YOU REQUIRED TO UNDERGO ANY TESTING TO QUALIFY FOR PEMAZYRE?	"Only the biomarker testing that had already been done."	"The testing that I had done was used."	"Only the biomarker test."	"My biopsy was enough."	"The biopsy results were good enough."	"Just the initial biomarker testing."	"Original biopsy testing was good enough."	"The biopsy results were enough."	"No."	"No. The testing I had done already was good enough".	"No. the biopsy results were enough."	"No further testing needed."
E. DID YOU HAVE TO WAIT LONG FOR THE TEST RESULTS TO BE GENERATED? DID YOU EXPERIENCE ANY STRESS OR ANXIETY AS A RESULT OF THAT WAIT?	"I felt anxious. Probably because I knew there was only one more chemotherapy that might be used."	"Waited about 1 month for the results. I did not feel stressed."	"Within a month. I didn't feel anxious."	"2 or 3 weeks. I was not anxious."	"I remember it was quick. I didn't feel anxious as I didn't really understand the cancer yet."	"It was quick. I did not feel anxious."	"Don't remember but I wasn't anxious."	"Do not remember. I was not anxious."	"I don't remember. I was still thinking that they would be able to operate and remove the tumour, so I wasn't worried."	"I don't remember. I am always nervous and anxious."	"I don't remember."	"I waited 5-6 weeks for the results, and I was feeling anxious."

12. WERE YOU ABLE TO ACCESS PEMAZYRE?	"No. It was too expensive." **Late note:" As of Nov 14, the Ontario government is going to cover the cost of the drug. I should start soon"**	"Yes."	"Yes. The hold up was the funding. My husbands' benefits covered it, but it took them awhile to realize that Pemazyre was an actual medication. My husband had to battle a bit for coverage but in the end, I was covered."	"Yes."	"Yes."	"Yes."	"Yes."	"Yes."	"No. It is very expensive to pay for out of pocket." **Late note: "As of November 8, my doctor was able to prescribe it for me. It is now covered under the Ontario government. I will keep in touch about how I am feeling."**	"Yes."	"Yes. It was easily accessed through the POG program from Incyte."	"I am unable to access the drug yet." **Late note: November 30, "I am still waiting for the paperwork to go through so I haven't started it yet."**
13. HOW DID YOU ACCESS PEMAZYRE? WAS IT THROUGH A CLINICAL TRIAL, COMPASSIONATE ACCESS PROGRAM, PRIVATE INSURANCE OR PROVINCIAL GOVERNMENT REIMBURSEMENT?	"Not able to access. Ontario is not paying on a case-by-case basis, so I am hoping to access it now."	"Provincial government reimbursement. I live in Alberta."	"Private insurance."	"We paid although there was a break with compassionate access program, it was still expensive. We did a Go Fund Me campaign."	"Provincial government reimbursement except that I didn't pay anything. It was just covered."	"I accessed through private insurance."	"Paid for it ourselves." **Late note: Mid-November "My physician is looking into whether or not I can switch and have the Ontario government pay instead of us paying out-of-pocket."**	"Compassionate access program."	"I have not been able to access it yet."	"I obtained it through the compassionate access program."	"It was either a clinical trial or compassionate access program."	N/A
14. A. WHEN DID YOU RECEIVE PEMAZYRE (DATE)?	N/A	September 30, 2024	Mid October, 2023	May, 2024	June, 2024	January, 2024	"August 17, 2023. I had taken a month off from chemotherapy to Pemazyre."	"October, 2022 (right after Thanksgiving)."	N/A	"I first had Pemazyre in April 2022. There is also a trial for the drug as well."	December, 2022	N/A
B. AND IN WHAT LINE OF THERAPY (FIRST, SECOND OR THIRD)	N/A	"This is my first line targeted therapy."	"Second line therapy, first-line targeted therapy."	"First-line targeted therapy."	"First -line targeted therapy."	"Second-line therapy, first-line targeted therapy."	"Fourth-line chemotherapy, first-line targeted therapy."	"First-line targeted therapy, second-line treatment."	N/A	"This was my first-line targeted therapy."	"It was second-line treatment, first-line targeted therapy."	"It will be my third line of treatment but my first-line targeted therapy if I can access it."
C. HOW MANY CYCLES OF PEMAZYRE DID YOU RECEIVE ALTOGETHER?	N/A	"I am on my second cycle now."	"10 cycles."	"4 cycles."	"I am on my 5th cycle and still taking the drug."	"I am still on it and have received 10 cycles already."	"I am still on Pemazyre. I have been on it since August 2023 and still on it "	"I am still on Pemazyre. I have had 35 cycles (745 days on therapy)."	N/A	"I had Pemazyre from April 2022 until December 2023.	"I am on my 28th cycle."	N/A

15. ON A SCALE OF 1-10, HOW WOULD YOU RATE YOUR QOL WHILE ON PEMAZYRE? (1 BEING POOR AND 10 BEING FABULOUS). PLEASE EXPLAIN.	N/A	"An 8. I have amazing energy and cardio-wise, I can run up the stairs and walk uphill without any problems. I have only had one bout of unwellness which lasted only a few hours and then stopped. Even my husband has noticed the difference. My appetite is 10 out of 10."	"It was a 10. I felt normal. Fatigue was gone. People couldn't tell that I had cancer."	"10. I felt normal. I had more energy. We were able to go for walks, have dinners out."	"Presently a 7. For the first 3 cycles, I felt great, and I had energy, and it would have been a 10. Then I had a surprise surgery as my bowel got pinched in a hernia in my diaphragm. That surgery was in August 2024. Since that surgery, I am still recovering. I have chronic pain which is worse in the evening." "Following surgery I was sleeping 18 hours/day. I am back on the Pemazyre and am now on my 5th cycle."	"10. I love Pemigatinib. I feel normal, have so much energy, and have returned to work (I love my job). My tumors shrunk for the first 3 months, and now they are stable."	"9. When I first went on Pemazyre, I took the full dose as prescribed. In January 2024, my joints in my back and legs were so sore I couldn't walk. My eyes were also really dry. We suspended the treatment for 5 weeks. During those 5 weeks, I took steroids, went to physio, and had acupuncture. I went back on Pemazyre at a lower dose and take the drug for one week, and then go off for one week. I feel great. I have more energy. I am walking 3 km/day. I still get tired, but I can do things like I did before. I help my husband do chores, cooking, cleaning and laundry around the house now."	"10. This drug was an energy restorer. I felt normal again. No longer needed to sleep during the day. I even took up pickleball."	N/A	"I would give it a 6 or 7. We played around with the dose. I was on the low dose most of the time. I was living an active life. I was still working. Every day was a bit different depending on where I was in the cycle. I was doing my best to live a normal life even though I had symptoms."	"An 8. Sometimes I am tired and have some ocular issues, (I do see the eye doctor every 6 weeks). My energy levels are good, and my appetite is good."	N/A
16. A. HAVE YOU EXPERIENCED ANY SIDE EFFECTS WHILE ON PEMAZYRE?	N/A	"Yes."	"Yes."	"Yes."	"Yes."	"Yes."	"Yes."	"Yes."	N/A	"Yes."	"Yes."	N/A
B. IF SO, WHAT ARE THOSE SIDE EFFECTS?	N/A	"Itchy skin, dry eyes and pain on both sides of the nails on my hands. Also, my hair has started to thin."	"Eyelashes grew longer and my hair was thinning out. I lost some hair."	"I still had some nausea and vomiting but controllable. My hair thinned out and my eyelashes grew longer."	"I have mouth sores, my taste is off, my appetite is poor, thinning hair and two of my toenails turned black."	"I have had some muscle cramping, swelling, and my hair is trying to grow back but is wispy. I had ingrown toenails but my doctor showed me how to cut my toenails so that wouldn't happen, and it works."	"On the higher dose, I had sore joints and could hardly walk but that has gone away with a lower dose. I do experience dry eyes, and I do have my eyes checked on a regular basis."	"Some of my fingernails and toenails have separated from the nail beds. Hair is thinning. There seems to be a cyclic reaction: on my week off, my fingers are more sensitive, food doesn't taste as well, and my phosphorous levels go high."	N/A	"My hair fell out, my nails kept falling off. My feet hurt so bad but did improve over time. I had joint and muscle pain, dry eyes (ingrown eyelashes) and a dry mouth. I lost weight and lost my appetite at times."	"I have experienced fingernails getting darker (a few months ago), I can get some confusion and cognitive flaws, and I am not as sharp as I used to be."	N/A

17. WHY DID YOU HAVE TO STOP YOUR FIRST LINE OF TREATMENT?	"I haven't taken Pemazyre yet. But I have been off chemo since June 2024 and I have a new tumor in my right lobe, according to the latest CT scan."	"My kidneys and bone marrow started reacting to the chemo. I was nauseated all the time. Chemo was delayed a few times because of this."	"I stopped the gem-cis-durva because my numbers started to go up."	"The drugs stopped controlling the tumors and they started growing again."	"My doctor thought it was too hard on me and decided it was time to change treatments. Plus, the MRI showed a mixed result."	"It was no longer effective. The tumours were showing some growth."	"The tumour was growing, and I was really sick."	"My CA19-9 numbers started to climb. The tumour activity was increasing."	"I had to stop the chemotherapy because the tumour board said it should be stopped. My counts were low."	"I stopped the Gem-cis treatment as it quit working."	"The doctors wanted to try Pemazyre as it was felt it wouldn't be as taxing on my body as chemo was."	"There was a recurrence (while on capecitabine)." "Gem-cis-durva kept my tumour stable but my WBC and platelets were plummeting." "There was tumour growth with both Durvalumab alone and FOLFOX."
18. HOW WAS THE RESPONSE CONFIRMED TO PEMAZYRE? DID CLINICAL SYMPTOMS IMPROVE OR RESOLVE? HOW WAS IT MEASURED? CT SCANS, BLOOD WORK...	N/A	"Yes, clinical symptoms improved. Still have some issues with my kidneys. My blood work improved, although I have a slightly elevated phosphate which I am being careful about." **Late note: November 29, 2024,** she had a CT scan on November 20 and it showed **"For the first time ever, my tumours in all areas (liver, lungs, lymph nodes) have shrunk by approximately 25%. Never on chemo did my tumors shrink. So, this is definitely positive."**	"CT scans and blood work confirmed the cancer was improving."	"Clinical symptoms resolved for the most part. The ultrasound and my numbers (blood work) showed the tumor was shrinking."	"The CT scan shows that the satellite tumours are stable. Numbers are coming down in my blood work. Phosphorus is on the high side, so we are watching that."	"The energy that I have is incredible. I feel normal again. Blood work and ultrasounds show improvement."	"When I first went on Pemazyre, the CT scans showed shrinkage of the tumour by 1cm in the first 3 months. There was still shrinkage in the next CT scan. The CT scan in July showed that the tumour was stable. I just had another CT scan but don't know the results yet. My blood work showed things were stable."	"It was unbelievable. Within two weeks, my CA19-9 dropped from in the 800s to 73. I felt fabulous and had energy again."	N/A	"The CT scans showed NED. My CA19-9 levels dropped and stayed down."	"My tumour markers dropped significantly from 4200 to 60. My CT scans are stable."	N/A
19. WHAT WAS YOUR RESPONSE TO PEMAZYRE? AN OBJECTIVE RESPONSE, LIKE A PERCENTAGE OF SHRINKAGE?	N/A	"I have a CT scan next week."	"The tumors in my lungs decreased in size by 30%. Liver was stable."	"I don't have the percentage but there was shrinkage."	"The tumours are stable."	"The tumours did shrink in the first 3 months. The report on lung tumours went from innumerable to numerous."	"Shrinkage of the tumour."	"CT scans showed stability, and my CA19-9 numbers dropped."	N/A	"The CT scans showed NED, and my CA19-9 levels dropped."	"The tumours remained stable, and my blood tumour markers dropped significantly."	N/A

20. DID YOU EVER HAVE TO STOP PEMAZYRE? IF SO, WHY?	N/A	"Just started a month ago, so I haven't had to stop yet."	"Yes, the numbers started going up again."	"Yes, after 4 cycles. It was not working any more. I had bloating, constipation and the cancer progressed to my lymph nodes, bones and lungs."	"Yes, I had to stop it when I had emergency surgery. I am back on it now."	"I have not had to stop Pemazyre yet."	"I had to stop for 5 weeks in January 2024. I had dry eyes, and my joints were so sore, I couldn't walk. I had physio, acupuncture and steroids, and after 5 weeks, I went back on the Pemazyre."	"I stopped for 1 week about 2 months (or 3 cycles) ago to give my fingers a chance to heal. After that week my CA19-9 numbers started to go up."	N/A	"I had to stop Pemazyre in December 2023. I had SBRT in January 2024. I started FOLFOX in April 2024 because there was metastasis in my lungs, liver, lymph nodes and peritoneum. On the FOLFOX, my scans show shrinkage and some lesions are stable. Oxaliplatin was removed from the FOLFOX regimen. I tried Durvalumab which was ineffective. I am now looking at clinical trials for Tinengotinib in Europe."	"I have never stopped Pemazyre but have lowered the dose that I am taking."	N/A
21. HAS PEMAZYRE BEEN EASIER TO USE THAN PREVIOUS THERAPIES? WHY OR WHY NOT?	N/A	"Absolutely it is easier to use. It is oral, and I can live more of a normal life. It is not invasive so no more IVs, less blood work, timewise less time in the clinics. I don't see the doctor every 3 weeks. I just see the medical oncologist every 9 weeks. I am seeing the eye doctor every month and if things look good, we will drop that to every 2 months. I am seeing the dietitian regarding foods high in phosphate and how to avoid them."	"Yes. It is a pill (oral medication). I didn't have to go to as many appointments (from 10 to 2 in a month). It gave me a lot of freedom. We could make plans, and we even went on a holiday."	"Yes. It is a pill. My number of appointments decreased. When blood work was done, it was a quick appointment."	"Yes. It is simple and convenient. A pill is all I take. Weekly blood work, decreased appointments and travel."	"Yes, I take a pill and don't have to go in for chemo. Chemo used to be a full-day event. I have fewer appointments too."	"Definitely. It is pill form; easier to take. I don't have to sit for hours in the chemotherapy room. I do not feel sick or weak after Pemazyre."	"Yes. Just one pill a day. The system for delivering the medication is great as well – home delivery."	N/A	"It was easier because it was a pill."	"It is much easier. It can be taken at home; it is oral and fewer trips to the hospital. There are less side effects, psychologically more sound, mentally less taxing and my quality of life is more functional and more joyful."	N/A

22. HOW HAS YOUR JOURNEY IMPACTED YOUR CAREGIVER/FAMILY? PLEASE EXPLAIN.	"I was the caregiver for my mother, and she died on November 6, 2022. All my time was spent working full time and caring for her. I felt totally alone, my dad had passed 10 years previously." "I don't have any other family. When I thought I was going to have a liver transplant, I reached out to my cousins. What a beautiful thing to be reintroduced to my first and some second cousins."	"My husband went to part-time work from full-time work. His pension will be affected. I am on long-term disability, and I had to quit earlier so my pension is also affected. Financially we are okay unless we have to go to the USA for treatment. Your perspective changes on what is important."	"It has been hard on him. He still has to work. His work has been very understanding and allowed him to take me to my appointments when needed. He worries. We have been married for 23 years."	The patient's brother was in the room and so he was asked. "Mentally-experiencing what family member is suffering. You ask yourself 'What can I do to help her?' 'Is what I am doing, enough?' State of mind-sadness, and cannot imagine what she is going through." "Took some time off and tried to balance work with family and Help look after my sister." "Her husband was stressed. He has his own grief." "Travelling back and forth from Toronto to be with family. Luckily there is support from both sides of the families."	"My family are such a good support system. My daughters are strong about it. My husband is always optimistic. We have a strong faith and live by the belief that even when we leave this world, we will see each other again. My younger sister struggles with it, probably because she has breast cancer."	"My husband has had to take on more responsibilities of mine, like childcare and household chores. He has had to take time off work. He loves researching and has looked up everything we find on pancreatic cancer and now cholangiocarcinoma. One of my children was bullied at work, and the other child said, 'At least my mother isn't dying.' We have been open and truthful with the children from the start."	"My husband is worried. When I was on the chemotherapy, he was doing everything. Now that I am on Pemazyre, we share the chores together. Financially it is a burden as we are spending our savings on medications. It is getting tight."	"My husband is pragmatic. He is very helpful and took good care of me after my chemotherapy. He said that it is hard watching me go through this cancer journey and helps in any way he can to alleviate my side effects. My children have also helped drive me to the chemotherapy appointments."	"It has been traumatic. I was very independent before this cancer. My husband is 83 years old and has to take over all of the driving and help me with bathing and dressing. Our daughter lives with us, and they both cook. We have someone come in to clean the house every 2 weeks."	"This has definitely impacted our lives. My husband married me 1 month after my liver resection. He is afraid; his dreams have changed. One thing he wanted was a big family."	"It has been hard on my wife and my parents. Parents call me a lot and I visit them in Vancouver every 2-3 months. My wife transports me to wherever I must go, she has to do everything, she works outside the home because someone has to pay the bills. She is my everything."	"My family has been impacted hugely. My sons don't really like to talk about it although I give them opening and space to talk. My husband is stressed. He holds a CFO position and had a side business – a tax consulting business, which he had to sell because it was just too much. He has had to do more work around the house and with the kids."
23. WAS IT WORTH ACCESSING PEMAZYRE? WHY OR WHY NOT?	N/A	"Definitely worth it. Quality of life, time you get back (not going to the clinics) and desire to do things and family notices the improvement in your life."	"Yes, it was. Life was so much better."	"Yes. We tried all other options. When we tried this option, it worked!"	"Yes. I think that everything is worth a try, and you have nothing to lose by accessing Pemazyre."	"Yes. My quality of life is so much better. I rarely think about cancer every day now."	"Yes. There is no other choice. My quality of life improved."	"Yes. 100%. First time I had any hope at all. It made me realize that there is ongoing hope. Fantastic!"	N/A	"Yes. It bought me two years."	"Yes. Because it was very effective, and the program covered the cost of the drug. It gave me life longer than expected. I have less side effects than with chemo."	N/A

24. DID ACCESSING PEMAZYRE ALLOW YOU TO FULFILL OR ACCOMPLISH ANYTHING IN LIFE THAT YOU WOULD NOT HAVE BEEN OTHERWISE TO DO, HAD YOU NOT ACCESSED THIS THERAPY? IF YES, PLEASE EXPLAIN WITH AN EXAMPLE.	N/A	"It is early days. Being on Pemazyre allows me to think of the possibilities of taking a trip or doing more in my daily activities."	"We took a holiday. If I hadn't been able to access Pemazyre, I don't know if I would be around today. I extended my life."	"It gave us a chance to have some quality time together. We were allowed to go for walks, have dinners out, and plan things."	"Difficult to answer. I do not feel like I have failed anything or missed out."	"Yes. I got to go back to work. I love my job!"	"Yes. I took a 3-week trip to Italy. I never thought I would be able to do that again."	"Yes. I took up a new sport: pickleball." "My mother was ill, and it allowed me to look after her until she died a year ago. She was upset when I was diagnosed because children are not supposed to die before their parents. This drug allowed me to spend time with her and help her through her last years of life." "I am so appreciative of that. I also help with refugees. We sponsor families, and it was important to be able to keep that up." "My first grandson was born a year ago, and I lived to see and hold him, which was really important to me and my son."	N/A	"I continued working. I had a baby. We were able to take a trip to Canada."	"I have been able to go on longer trips, exercise, more concentration when I read or watch TV. I socialize more effectively, and I am more independent health wise."	N/A
25. WHAT IMPROVEMENTS WOULD YOU LIKE TO SEE IN THIS DRUG THERAPY THAT ARE CURRENTLY AVAILABLE IN OTHER DRUG THERAPIES?	"Cost / affordability"	"Accessibility and affordability. There is no standard protocol. Better communication and consistency in the treatment plan. I noticed that someone I have met who is on Pemazyre has a different schedule for blood work and accessing the eye doctor and dietitian."	"Accessibility and affordability."	"Doctors should know what drugs are available to help patients." "Accessibility." "Affordability."	"Cost, accessibility." "If there is a drug that the USA is using, then we should be considering its use."	"Accessibility and cost."	"Decreased cost so it is more affordable for everyone. Accessibility – make it accessible for everyone who needs it."	"Accessibility and affordable for everyone."	"I really want to access this drug. Cost and availability are two improvements that have to be made."	"Accessibility and cost for patients."	"I would like to see it more accessible and affordable to everyone who needs it."	"I would like to see it more accessible and less costly."
26. DO YOU BELIEVE THAT PEMAZYRE HAS DESIRED IMPROVEMENTS IN THERAPIES FOR CHOLANGIOCARCINOMA? WHY OR WHY NOT?	"I believe it does, but I don't have firsthand experience because I am unable to access it."	"I believe that it has desired improvements in therapies because Pemazyre is a targeted therapy instead of chemotherapy which is systemic. Pemazyre goes after the tumor cells with the specific biomarker."	"Yes. It extends your life in a way that you feel normal."	"Certainly. Based on my sister's experience, there is an increase in quality of life, and a longer chance at living."	"I think so. It is a targeted therapy, specific for biomarker FGFR2 fusion."	"It's much easier on your life and body than chemotherapy is."	"Yes. The treatment is in pill form and easy to take. Not always reminded that you have cancer as you stay away form the hospital. It is depressing always going to the hospital."	"Yes. It is one pill a day. The quality of life is fabulous. You feel normal and can carry on with your daily activities. It also either decreases the tumour size or keeps the tumor stable. It gives you hope."	"Yes. I really want to access this drug. I am finding out more about this drug through reading about peoples' stories."	"Yes. The time that I got (the extra 2 years) from being on the drug that I wouldn't have had otherwise. It gave me hope!"	"Yes. It reduced inflammation, my tumour markers improved. My pain (discomfort)and suffering ended that I had with chemo."	"I am hoping so which is why I want to access it."

27. DO YOU WISH TO ADD ANYTHING ABOUT WHY ACCESSING PEMAZYRE IS SO IMPORTANT TO BILIARY TRACT CANCER PATIENTS AND CAREGIVERS?	"It is clear that this drug is very likely going to extend my life significantly. It could buy me time for other valuable therapies to come online in the future. To have quality of life, I need to have hope. and the hope of accessing this drug keeps me going."	"Pemazyre is the only targeted therapy that cholangiocarcinoma has, and it is only for one specific biomarker. We need more targeted therapies."	"Changes your life and gives you HOPE!"	"This is important because it targets what it is supposed to (tumor versus systemic with chemo). Improves quality of life for patients!"	"It is important because right now, this is the first targeted therapy for cholangiocarcinoma patients! With this cancer, Canadians have few options that will give patients a fighting chance at living."	"There are no other options. Everybody that needs this drug should receive it. Everyone should be treated for biomarkers when they are diagnosed, or at least at the beginning of their cancer treatments."	"I want this drug to be available to everyone who needs it. There should be no cost associated with being alive."	"With this cancer, you are faced with terrible things. Knowing that you are going to have help covering the cost of Pemazyre is huge. It is not fair that everyone cannot access this drug. It provides a huge life enhancement."	"I am finding out more about the drug. I have been reading stories about people's experiences on the drug, and I am a fighter."	"The Hope. It buys time until more treatments and therapies can come out or be discovered and offered."	"It improves quality of life, prolongs expected life span with minimal side effects, is easy to administer and gives me hope. It extends my life to hopefully a new clinical trial so I can live longer."	"In Canada, the standard of care for cholangiocarcinoma is limited. We need hope."

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PC0391-000
Generic Drug Name (Brand Name): Pemigatinib (Pemazyre)
Indication: For the treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma (CCA) with a FGFR2 fusion or other rearrangement.
Name of Clinician Group: The Canadian Gastrointestinal Oncology Evidence Network (CGOEN) and other cholangiocarcinoma-treating physicians
Author of Submission: Dr. Vincent Tam, Medical Oncologist, Arthur Child Comprehensive Cancer Centre, Calgary.

with

Dr. Jennifer Knox, Medical Oncologist, Princess Margaret Cancer Centre, Toronto.
Dr. Brandon Meyers, Medical Oncologist, Juravinski Cancer Centre, Hamilton.
Dr. Ravi Ramjeesingh, Medical Oncologist, Dalhousie University, Halifax.
Dr. Petr Kavan, Medical Oncologist, McGill University Health Centre.
Dr. Jennifer Spratlin, Medical Oncologist, Cross Cancer Institute, Edmonton.
Dr. Rachel Goodwin, Medical Oncologist, The Ottawa Hospital Cancer Center, Ottawa
Dr. Hatim Karachiwala, Medical Oncologist, Cross Cancer Institute, Calgary.
Dr. Ralph Wong, Medical Oncologist, Winnipeg
Dr. Shaqil Kassam, Medical Oncologist, Southlake Regional Health Centre, Newmarket
Dr. Stephen Welch, Medical Oncologist, Medical Oncologist, London Health Sciences Centre.
Dr. Janine Davies, Medical Oncologist, BC Cancer Agency, Vancouver
Dr. Eve St. Hilaire, Medical Oncologist, Dr-Léon-Richard Oncology Center, Moncton.
Dr. Zachary Veitchz, Medical Oncologist, Royal Victoria Regional Health Centre, Barrie.
Dr. Arndt Vogel, Medical Oncologist, Princess Margaret Cancer Centre, Toronto.
Dr. Daniel Breadner, Medical Oncologist, London Regional Cancer Program
Dr. Michael Raphael, Medical Oncologist, Sunnybrook Health Sciences Centre, Toronto.

1. About Your Clinician Group

The Canadian GI Oncology Evidence Network (CGOEN) is a virtual and inclusive network of Canadian GI Oncology clinicians who contribute to the knowledge of GI cancer and its treatments, including participating in clinical trials, conducting observational research, and involvement in local/provincial and national clinical guideline development and health technology assessment. Some members of the clinician group participating in this submission are members of the International Cholangiocarcinoma Research Network (ICRN), a global collaboration of researchers and research centres working to improve knowledge about cholangiocarcinoma etiology, prevention, early detection, treatment, and prognosis. https://cholangiocarcinoma.org/international-cholangiocarcinoma-research-network/

Also, some members of this clinician group are members of the Canadian Cholangiocarcinoma Collaborative which was founded to change how patients with cholangiocarcinoma receive and access integrated research and care in Canada.

https://www.cholangio.ca/

2. Information Gathering

Information gathered for this submission was based on relevant data from the FIGHT-202 trial and expert evidence-based review by Canadian gastrointestinal cancer specialists

3. Current Treatments and Treatment Goals

Cholangiocarcinoma (CCA) is a heterogeneous group of uncommon, fatal malignancies arising from the biliary tract with limited treatment options. The true incidence of CCA is not known because of difficulties in establishing diagnosis. The prognosis of CCA patients with metastatic disease is poor, with a median overall survival of around one a year, and a five-year survival rate of < 20%

While surgical resection with negative margin offers the only potentially curative option, the majority of patients present at locally advanced or metastatic stages when surgical resection is not feasible. The incidence of CCA has increased globally over the past few decades, and the mortality rate remains high due to the aggressiveness of the disease and resistance to medical treatment.

With traditional chemotherapy regimens demonstrating limited effectiveness in CCA, research has focused on targeted treatments.

Standard treatment options for unresectable (including metastatic and recurrent) bile duct cancer include palliative chemotherapy, immunotherapy, targeted therapy and other modalities of therapy.

Systemic chemotherapy with immunotherapy is appropriate for select patients with the combination of cisplatin plus gemcitabine (CisGem) plus durvalumab or pembrolizumab being the current standard of care first-line therapy. Cisplatin may also be substituted by oxaliplatin or carboplatin in cases of renal impairment or neuropathy.

Second-line treatment usually consists of a fluoropyrimidine-based chemotherapy regimen such as FOLFOX, capecitabine or FOLFIRI. There is evidence of a small survival benefit with second-line FOLFOX compared to active best supportive care based on the ABC-06 study.

Despite recent advances, the moderate survival benefit provided by CisGem+durvalumab or CisGem+pembrolizumab has motivated much research aimed at identifying more effective treatments in this setting.

Currently, agents targeting FGFR2 fusion and IDH1/2 mutations hold great promise for improving the management of CCA. Pemigatinib, a fibroblast growth factor receptor (FGFR) 2 inhibitor, received (accelerated) approval in April 2020 by the US Food and Drug Administration (FDA) in CCA patients harboring FGFR2 gene fusions or other rearrangements and is the first targeted therapy to be approved for the treatment of CCA.

Extending survival, delaying disease progression and maintaining quality of life while on therapy are goals of current research into new treatments for the management of CCA.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

While CisGem+durvalumab or CisGem+pembrolizumab are the standard of care first-line therapies for CCA, these regimens only offer moderate survival benefit with most patients reporting a median survival of just over 12 months. Second-line treatment with FOLFOX improved survival to only 6.2 months compared to 5.3 months with supportive care alone.

New treatments for metastatic biliary cancer are urgently needed to improve survival for patients with this devastating disease.

Currently funded second-line systemic treatments for patients with cholangiocarcinoma and FGFR2 fusions or rearrangements offer inadequate efficacy. New second-line treatments are required which have a meaningful survival benefit.

Pemigatinib is expected to offer patients improved efficacy in terms of survival, progression-free survival, response rate and disease control. As an oral drug, pemigatinib may also contribute to improved quality of life because it would require fewer visits by the patient to the cancer center, and no chair time for infusion.

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

The FIGHT-202 study was a phase 2 study which evaluated efficacy and safety of Pemigatinib in patients who had disease progression following at least one previous treatment. As such, it would continue to be appropriate to first treat patients with the standard of care front-line therapy before prescribing pemigatinib to CCA patients harboring FGFR2 gene fusions or other rearrangements.

It would also be reasonable to consider pemigatinib upfront for CCA patients deemed unsuitable for cisplatin/gemcitabine plus durvalumab or pembrolizumab as first-line therapy.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

The drug under review (pemigatinib) would benefit CCA patients harboring FGFR2 gene fusions or other rearrangements with an ECOG performance status of 0-2.

FGFR2 fusions and rearrangements are found almost exclusively in intrahepatic cholangiocarcinoma occurring in approximately 10% of these patients. This would represent a small group of patients in Canada and should be considered a rare cancer.

Intrahepatic cholangiocarcinoma (iCCA) has high frequency of actionable genomic targets including mutations in Fibroblast Growth Factor Receptor (FGFR), particularly FGFR2. Comprehensive genomic profiling (CGP), the backbone for precision oncology, opens the opportunity for tailored therapies such as pemigatinib.

Patients best suited for treatment need to be prescreened for FGF/FGFR status using DNA/RNA sequencing.

Biliary cancer patients without FGFR2 fusions or rearrangements should not be treated with pemigatinib.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

In clinical practice, the patient's clinical condition and CT imaging are used to determine whether a patient is responding to treatment. If a patient is symptomatic from their cancer and a treatment results in improvement in the symptom then this may be a surrogate marker of response. The most objective measurement is CT imaging to compare the sizes of the primary cancer and metastases. CT imaging response is used to assess outcomes in clinical trials and clinical practice.

Treatment response and tolerance of the treatment should be assessed clinically every 3 weeks and response should be assessed radiographically with CT imaging every 2-3 months.

A clinically meaningful response to treatment would be to achieve tumor control (response or disease stabilization) and to maintain or improve quality of life.

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

Patients would discontinue treatment if there is clear evidence of cancer progression on imaging, poor tolerance of the treatment which cannot be improved with dose delays or reductions, or patient preference to stop treatment.

5.5 What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

Pemigatinib can be taken at home as prescribed by a medical oncologist.

6. Additional Information

We acknowledge that the FIGHT-202 study which supports the use of pemigatinib in the second-line setting is a phase 2 study. A phase 3 study in this setting can not be performed anymore because the several FGFR inhibitors are approved by EMA and FDA and are in most countries considered as standard of care in second line treatment. Three phase-3 trials comparing FGFR inhibitors in 1st line have been stopped because of slow recruitment and the low frequence of FGFR2 fusions in iCCA.

Since the previous submission, a number of real world studies of pemigatinib in FGFR2 mutated CCA have been completed in Canada, the United States and Europe. All support the efficacy and safety of pemigatinib in real world patients.[1,2,3]

In addition, pemigatinib has now received a positive recommendation from INESS in Quebec, and is being offered on a case-by-case basis to CCA patients in Alberta and Ontario. NICE in the United Kingdom and the EMA in Europe have also approved pemigatinib for CCA with and FGFR2 fusion in 2021. This leaves Canada's public health care system as one of the few public systems around the world to not universally provide pemigatinib to eligible CCA patients with an FGFR2 fusion.

FGFR2 mutation status will need to be assessed in cholangiocarcinoma patients being considered for pemigatinib. Currently there is funding for FGFR2 testing in the Canadian provinces of Alberta and Ontario. With respect to comprehensive genomic profiling (CGP), over 20 cancer therapies linked to over 15 genomic biomarkers have been approved in Canada, with many more quickly emerging. This emphasizes the growing value of precision medicine in cancer care and reinforces the need for all Canadians to have access to these therapies **and** the molecular tests needed to prescribe them. A plan for publicly funding CGP in patients with cancer is crucial for enabling our healthcare system to keep pace with rapidly evolving molecular testing needs.[4]

<u>Considerations for Significant Unmet Need</u>

Cholangiocarcinoma is a rare cancer. As such we urge CADTH to apply the recommendations framework that includes Considerations for Significant Unmet Need as described in the Procedures for CADTH Reimbursement Reviews (March 2022), section 9.3.1.

We also urge CADTH/ to transparently report (in the draft recommendation) how the considerations for significant unmet need contributed to the draft recommendation.

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[1] Ding P, Tam V, Ramjeesingh R, Asselah J, Sheffield B, Mitchell T, Turpin K, Gaudreau A, Knox J, Cheung W. Pemigatinib in the real-world management of cholangiocarcinoma (CCA) through a Canadian patient support program (PSP). Cholangiocarcinoma Foundation 2024 Annual Conference, Salt Lake City, UT.

[2] Parisi A, Delaunay B, Pinterpe G, Hollebecque A et al. Pemigatinib for patients with previously treated, locally advanced or metastatic cholangiocarcinoma harboring FGFR2 fusions or rearrangements: A joint analysis of the French PEMI-BIL and Italian PEMI-REAL cohort studies. Eur J Cancer. 2024 Mar;200:113587. doi: 10.1016/j.ejca.2024.113587. Epub 2024 Feb 6. PMID: 38340384.

[3] Saverno K, Zimmerman Savill KM, Brown-Bickerstaff C, Kotomale A et al. Real-world use of pemigatinib for the treatment of cholangiocarcinoma in the US. Oncologist. 2024 Aug 21:oyae204. doi: 10.1093/oncolo/oyae204. Epub ahead of print. PMID: 39173023.

[4] Impact Mediocom Inc with Lim, H., Sheffield, B., Karachiwala, H.,Leighl, N., Doherty, M., Sehdev, S., Slater, J. DETERMINING PRIORITY ACCESS TO COMPREHENSIVE GENOMIC PROFILING FOR CANADIAN PATIENTS WITH CANCER https://www.impactmedicom.com/publications/reports

7. Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

1. Did you receive help from outside your clinician group to complete this submission? If yes, please detail the help and who provided it.

   NO

2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission? If yes, please detail the help and who provided it.

   NO

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. **Please note that this is required for each clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician

Name: Andrea Molckovsky
Position: Medical Oncologist, Grand River Regional Cancer Center
Date: 20-11-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 2: Conflict of Interest Declaration for Clinician 2

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Name: Brandon Meyers
Position: Medical oncologist
Date: 18-11-2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
AstraZeneca	x			
Ipsen		x		
Roche		x		
Incyte	x			
Bayer	x			

Declaration for Jennifer Spratlin

Name: Jennifer Spratlin
Position: Associate Professor, University of Alberta; Medical Oncologist, Cross Cancer Institute
Date: November 19, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Incyte advisor	x			
Astrazeneca advisor	x			
Taiho advisor	x			
Ipsen advisor	x			
BMS advisor	x			
Astellas advisor	x			
BOLD advisor	na			

Declaration for Clinician

Name: Janine Davies
Position: Medical Oncologist, BC Cancer- Vancouver
Date: 19-11-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 2: Conflict of Interest Declaration for Clinician 2

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Amgen	X			
Novartis	X			
Merck	X			
Eisai	X			
Taiho	X			

*

Name: Ravi Ramjeesingh
Position: Medical Oncologist
Date: November 18, 2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
AstraZeneca		X		
Amgen	X			
Roche	X			
Incyte		X		
Eisai		X		
Ipsen	X			
Merck	X			
Jannsen	X			
Pfizer	X			
Novartis	X			
Knight	X			

Declaration for Zachary Veitch

Name: Dr Zachary Veitch
Position: Medical Oncologist
Date: 12-12-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Novartis (ad board/consulting)	x			
Merck (ad board/consulting)	x			
Novartis (research support)				X
Gilead (Ad board/consulting)	x			
Ipsen (ad board/consulting)	x			
Az (ad board/consulting)	x			
Amgen (ad board/consulting)	x			

Declaration for Clinician

Name: Daniel Breadner
Position: Assistant Professor and Medical Oncologist, Schulich School of Medicine and Dentistry/Verspeeten Family Cancer Centre, London, Ontario, Canada
Date: <DD-MM-YYYY>

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Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
AstraZeneca		x		
Merck	X			
Bayer	X			
Janssen	X			
Roche	X			
Amgen	X			

BeiGene	X			
Guardant Health	X			
Takeda	x			

Declaration for Rachel Goodwin

Name: Rachel Goodwin
Position: Medical Oncologist
Date: November 18, 2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1 (from last 5 years)

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $5**
Novartis	x			
Ipsen		x		+Independe Education Gra
Pfizer		x		+Independe Education Gra
Amgen		x		
Roche	x			
Merck	x			
AstraZeneca	x			
Taiho	x			
Apo	x			
Eisai	x			
BMS		x		
Astellas	x			

Declaration for Vincent Tam

Name: Dr. Vincent Tam
Position: Medical Oncologist, Arthur Child Comprehensive Cancer Centre
Date: 14-11-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Incyte		x		
AstraZeneca			x	
Merck	x			

Declaration for Clinician

Name: Hatim Karachiwala
Position: Medical Oncology
Date: November 18, 2024

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Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Astellas		X		
Takeda		X		
Pfizer		X		
Eisai		X		
Amgen		X		
Roche	X			
Tahio		X		
Merck		X		
BMS		X		
AstraZeneca		X		

Declaration for Jennifer Knox

Name: Dr. Jennifer Knox
Position: Medical Oncologist
Date: 18-11-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Roche (research support)				x
Ipsen (research support)				x
Merck (research support)				x
AZ (research support)				x
Roche (Ad board/consulting)	x			
Ipsen (ad board/consulting)	x			
Az (ad board/consulting)	x			

Declaration for Eve St-Hilaire

Name: Dr. Eve St-Hilaire
Position: Hémato-oncologue, Centre d'oncologie Dr-Léon-Richard
Date: 18-11-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Name: Petr Kavan MD
Position: Medical Oncologist, Dpt of Oncology McGill University, Co-chair GI oncology Rossy Cancer Network McGill, CRP program director, LDI Jewish General Hospital McGill University
Date: November 19, 2024

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Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Merck		X		
Takeda	X			

Name: Ralph Wong
Position: Medical oncologist
Date: 18-11-2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000

Name: Vallerie Gordon
Position: Medical Oncologist
Date: 18 Nov 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 2: Conflict of Interest Declaration for Clinician 2

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Add company name				
Add company name	No declarations of COI.			

Cholangiocarcinoma Foundation®

Dear Reviewers,

The Cholangiocarcinoma Foundation (CCF) advocates for the reimbursement and availability of pemigatinib (Pemazyre) for Canadian patients diagnosed with fibroblast growth factor receptor 2 (FGFR2)- positive cholangiocarcinoma (CCA). As the leading global resource for cholangiocarcinoma research, education, and advocacy, we are compelled to address the pressing unmet needs of this cancer community.

Cholangiocarcinoma is an unforgiving disease with limited treatment options. For patients with FGFR2 fusions or rearrangements, treatment using pemigatinib represents not just an alternative but a chance at improved outcomes. The FIGHT-202 trial, while non-comparative, demonstrated a meaningful objective response rate of 35.5%. Patients on pemigatinib reported disease stability, symptomatic relief, and improved quality of life—factors directly translating to more time with loved ones and a better quality of life.

The challenges of generating robust data for ultra-rare cancers like FGFR2-positive CCA cannot be overstated. With cholangiocarcinoma already being rare and the FGFR2 population only constituting 8% of this population, designing and conducting randomized controlled trials in such a small patient population is almost impossible. Yet, the evidence supported by real-world patient experiences points to pemigatinib as a valuable treatment option. The drug's oral administration adds to its feasibility and convenience for patients already enduring significant physical and emotional burdens.

Canadian patients deserve equitable access to treatments that provide hope and time, just as patients in the US and in the UK where NICE guidelines are restrictive. The inability to access pemigatinib places an undue burden on individuals who are already navigating a challenging and isolating diagnosis. For these patients, everyday matters, and we urge you to consider the value of precious time that can be afforded to families.

We urge decision-makers to reconsider the recommendation and prioritize patient-centered care by making pemigatinib available to Canadians with FGFR2-positive CCA. This is an opportunity to address a critical unmet need and demonstrate compassion and commitment to those who often feel left behind by the healthcare system.

Thank you for your consideration. We can assist if you require further information, patient testimonials, or expert insights. Patients are our priority, and we stand ready to provide the data

and resources you need to make a fact-based yet compassionate decision to help your citizens in need.

With Urgency,

Stacie Lindsey

Stacie Lindsey
Founder & CEO

Juan Valle, MB, ChB, MSc, FRCP

Chief Medical Officer

Melinda E. Bachini

Melinda Bachini
Chief Patient Officer

Cholangiocarcinoma Foundation
5526 West 13400 South, #510 - Herriman, Utah 84096 - U.S.A.
curecca.org

November 11th 2024

Dear Canada Drug Agency,

I am a medical oncologist practicing in Kitchener, Ontario. My disease site specializations include GI cancers, and I treat approximately 8 to 10 patients with cholangiocarcinoma each year. I have been practicing at the Grand River Regional Cancer Center for the past fourteen years.

I was recently apprised that pemigatinib (pemazyre) is undergoing a review for reimbursement in Canada. I strongly support that this drug be reimbursed by provincial governments for second line treatment of patients with cholangiocarcinoma that harbor an FGFR2 fusion.

I am not going to reference the numerous reviews of the real-world use of pemigatinib in the cholangiocarcinoma population, since you must have access to all this evidence, and as a community oncologist I am not considered a disease site expert, by any means. Suffice to say that in the US and Europe, the FGFR2 inhibitor drug class is considered standard of care for second line treatment of cholangiocarcinoma after progression on cisplatin/gemcitabine/durvalumab chemotherapy, in patients whose somatic tumor testing demonstrates FGFR2 fusions (a test that is reimbursed by my provincial government in Ontario).

The purpose of my letter today is to outline my experience with pemigatinib, in two real patients who have been fortunate enough to access this drug. Both of these patients agreed to have their story shared with the Canadian Drug Agency for the purposes of having pemigatinib funded, although I will not include their names in this report.

Patient Case 1

My first patient story is that of a patient in her late 70s. She was diagnosed with unresectable intrahepatic cholangiocarcinoma in 2016. She responded well to first line chemotherapy with gemcitabine and cisplatin, and after six cycles of chemotherapy had stereotactic radiation to the primary liver mass in the hopes of controlling disease. The radiation worked for about 3 years, but in January 2021 her disease in the liver started to grow again.

We restarted first line gemcitabine and cisplatin in February 2021, and she completed 9 cycles. Her disease was controlled for a few months, but by November 2021 was growing again.

Repeat biopsy of her liver, organized through an academic center, revealed FGFR2 fusion in her cancer.

At that time, in early 2022, pemigatinib was available through a patient support program in Ontario. She was enrolled in the program and started on the drug in May 2022. She has required a couple of dose reductions and is currently on the lowest dose of 4.5 mg daily x 14

days, with 7 days off. However her CA19-9 normalized very quickly after starting pemigatinib, and her imaging shows ongoing response.

She has been responding to pemigatinib now for two and a half years, and is able to live her life fully, with minimal s/e aside from nail and hair changes.

One may argue that her disease has always behaved more indolently, given that she had relatively long disease free intervals while off chemotherapy. However I do not think she would have tolerated our second line regimen of folfox for the past 2.5 years, nor do I think she would have responded to chemotherapy for as long.

Patient Case 2

My second case is that of a 26 yo woman, who is now deceased from her cancer.

Patient 2 was diagnosed with metastatic cholangiocarcinoma at the age of 24, while pregnant, with multiple liver metastases. Biopsy revealed carcinoma, and upon further review it became clear this was a primary intrahepatic cholangiocarcinoma. She paid privately for somatic testing that revealed an FGFR2 fusion in her cancer.

She started chemotherapy with carbo-taxol weekly, which was chosen because it can be safely given during pregnancy, and being in her second trimester at the time of diagnosis her primary concern was to deliver a healthy baby. The chemotherapy was effective, and after she delivered her baby successfully, we switched her to standard first line chemotherapy with cisplatin/gemcitabine, and durvalumab.

She had a good response to first line cisplatin/gemcitabine/durvalumab, and was on this regimen from April 2023 until early 2024, when she experienced disease progression in her liver.

We could not obtain funding for pemigatinib at that time, and with her family's help, she started a Gofundme to try and raise funds to pay for the drug out of pocket. In the meantime, we started folfox chemotherapy, which she did not tolerate well, and a scan after only 4 cycles (8 weeks) showed clear progression.

She was admitted to hospital with a pain crisis at the end of May, during which time she started the pemigatinib. She had a radiographic response after 2 months of pemigatinib, but was progressing again at the 4 month mark. However she was able to function at home over the summer while she responded to the drug, and had a significant improvement in her quality of life over the two to three months when she responded. This was a real response, documented radiographically, and although brief, gave her an extra three to four months of life, with good quality, and those months were precious to her, and to her toddler.

She stopped the pemigatinib in September 2024, and although there is no standard of care 4th line regimen, we offered her weekly carbo/taxol again, but she did not respond and passed away recently from her disease.

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These two patient cases summarize the whole of my experience with pemigatinib, which admittedly does not make me an expert on this drug or speak clearly to its efficacy. I do believe that my second patient might have responded longer if she had started pemigatinib at the first sign of progression, because her burden of disease was that much greater while she progressed on folfox. She might have had time to look into a clinical trial with other FGFR2 fusion inhibitors, or even raised more funds to pay for a consultation and access other FDA approved FGFR2 fusion inhibitors in the US. Right now, given the recommendation against the funding of pemigatinib, I would wonder if there are any pharmaceutical companies looking to bring their oral FGFR2 inhibitors here, since I presume they believe that the funding environment is not in favor.

Therefore I believe that recommending the funding of pemigatinib is important and the right decision to make. I believe this because I have seen it work in my two patient cases. I have read the real-world evidence, and this is a standard second line therapy in other parts of the world. Finally, the approval of this drug would promote a welcoming environment for the introduction of even better targeted agents to Canada in the future.

Sincerely,

Andrea Molckovsky
Medical Oncologist
Grand River Regional Cancer Center
Kitchener, Ontario