NICE National Institute for Health and Care Excellence

Pemigatinib for treating relapsed or refractory advanced cholangiocarcinoma with FGFR2 alterations [ID3740]

Lead team presentation

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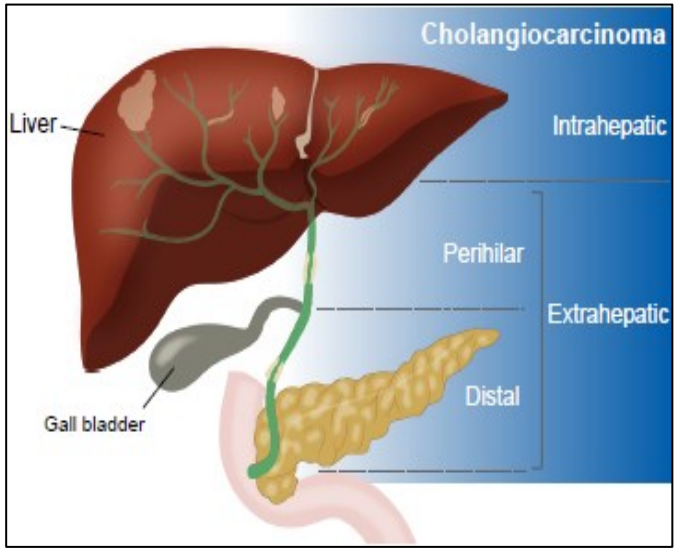
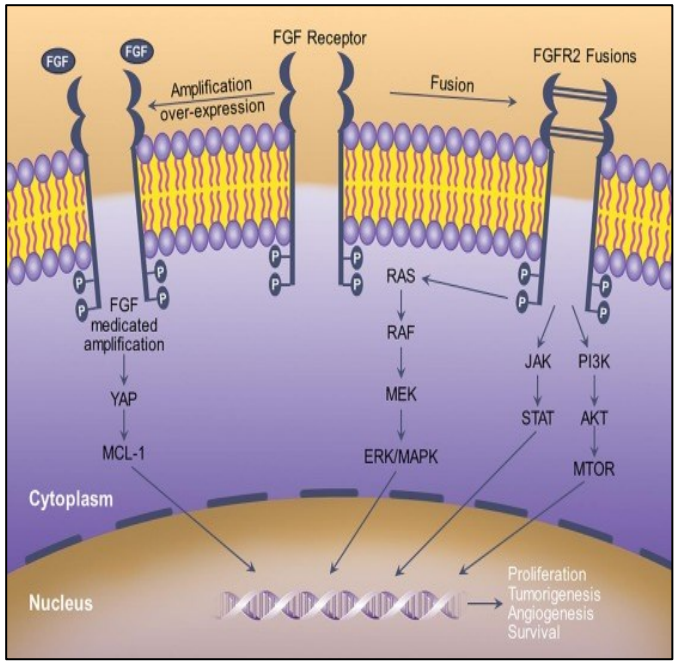
Company: Incyte Biosciences UK

ACM1: 13th April 2021

Disease background



- Cholangiocarcinoma (CCA) is a rare cancer.
- Develops from the epithelial lining of the bile ducts.
- CCA is the second most common primary liver tumour, after hepatocellular carcinoma.
- CCA is classified as either intrahepatic (iCCA) or extrahepatic (eCCA), based on the location of the primary tumour.
- There were 2,187 people diagnosed with CCA in England in 2017.



- Gene fusions have been shown to be drivers of tumour development.
- Fibroblast growth factor receptor 2 (FGFR2) fusions can cause tumour development in iCCA.
  - Genomic mutations involving FGFR2 activation account for nearly 10-20% of all iCCA
- Standard of care (SoC) for locally advanced or metastatic CCA is chemotherapy with a gemcitabine-based doublet ➔median overall survival (OS) of approximately 12 months

Pemigatinib (Pemazyre, Incyte Biosciences UK)

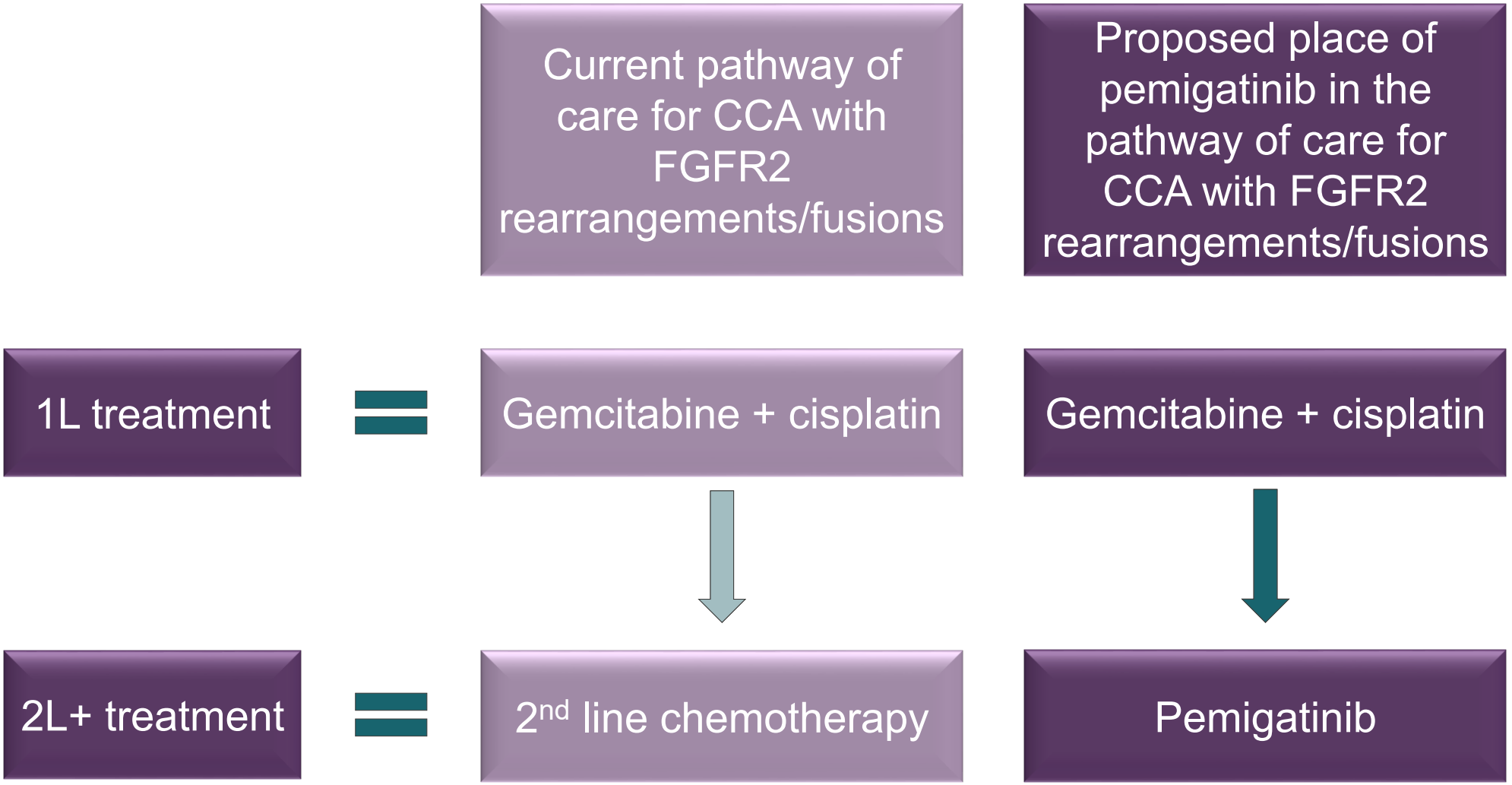
Mechanism of action	Pemigatinib is a potent and selective FGFR1, 2, and 3 inhibitor. Pemigatinib blocks autophosphorylation and activation of major FGF/FGFR signalling pathways, inhibiting the growth of cells with *FGFR2* fusions/rearrangements.
Anticipated conditional marketing authorisation	Treatment of adults with locally advanced or metastatic CCA with a FGFR2 fusion or rearrangement that have progressed after at least one prior line of systemic therapy (positive CHMP January 2021).
Administration	Orally, 13.5 mg once daily on a 14 day on, 7 day off schedule.
List price	£37.88 per mg (£511.36 per 1 tablet of 13.5 mg or £7,159.04 per 21-day treatment cycle or £124,430 per annum). The company has a patient access scheme. With the PAS the annual cost is estimated to be [redacted].

CCA: Cholangiocarcinoma; FGF; Fibroblast growth factor; FRFR: Fibroblast growth factor receptor

Conditional marketing authorisation can be granted if all of the following criteria are met:

- the benefit-risk balance of the medicine is positive;
- comprehensive data post-authorisation can be provided;
- the medicine fulfils an unmet medical need;
- the benefit of the medicine's immediate availability to patients is greater than the risk inherent in the fact that additional data are still required.

Treatment pathway – current and proposed



Source: adapted from company submission Document B, Figure 5.

Patient expert perspectives (1)

- For most patients, late diagnosis means inoperable cancer and a terminal diagnosis.
- Understanding the diagnosis and prognosis can be difficult for both patients and their carers. Third of patients under 70 at diagnosis* - many struggle to comprehend lack of effective treatment for their loved ones.
- Resection is the only potentially curative treatment there is for CCA.

"I went through endless tests; the doctors didn't know what was wrong with me. I lost valuable time."

"I was shell shocked. I didn't know who to turn to for help. I was alone."

"They told me surgery was my only chance of survival, but it might already be too late."

- Standard first line treatment for those with inoperable CCA is gemcitabine and cisplatin chemotherapy combination which has not been improved on for over a decade ➔ may or may not extend survival, at the expense of quality of life.
- With more effective treatments for many other cancers, learning that there is so little in the treatment of CCA, leaves patients and carers feeling confused, isolated and helpless.

NICE

*"Incidence, mortality and survival for people diagnosed in England with cholangiocarcinoma between 2001-2017" PHE/AMMF partnership

Patient expert perspectives (2)

- New and more effective treatments for CCA are desperately needed.
- Pemigatinib offers hope of extending survival over standard chemotherapies and/or best supportive care ➔ targets FGFR2 rearrangement.
- In UK, molecular profiling is available only via clinical trials, or privately ➔ It should be available for all those diagnosed with CCA so that patients eligible for targeted therapies such as pemigatinib can be considered in a timely manner.
- Time factor is an issue – need to diagnose CCA early enough for patient to be considered for this treatment.
- Plus, as an oral therapy there are QoL benefits over an intravenous therapy, including spending less time in hospital receiving treatment.

"There is a lack of centres of expertise for CCA patients, resulting in many patients losing their lives before undergoing any form of treatment plan."

"Molecular Profiling is critical to the future of CCA patients and needs to be offered at the time of diagnosis or 1st line treatments.."

Clinical expert perspective

- Cholangiocarcinoma is a rare tumour with incidence < 5/100,000 in UK.
- CCA treatment represents an unmet need. Median overall survival ranges between 6 - 24 months with the current standard of care (1st line chemotherapy with Cisplatin-Gemcitabine and a 2nd line chemotherapy)
- Expected median overall survival of advanced chemo-refractory CCA patients is 6 months.
- Pemigatinib would be considered for patients with advanced FGFR2-fused CCA, which includes 10-12% of all CCAs, after they have progressed to first line treatment.
- Pemigatinib would impact on:
  - quality of life - as symptoms from CCA often are mass-induced, a reduction in tumour volume will relieve symptom control / reducing neutropenia incidence, that can lead to need for hospital admissions / manageable toxicity profile

  - life expectancy (median OS 21.1 months vs 6 months)

  - reducing costs related to infusional therapy

  - reducing need for hospital visits (as Pemigatinib is an oral treatment)

  - increasing costs related to genomic profiling

FIGHT-202 trial (data cut-off, 07 April 2020)

- Single-arm, phase 2, open-label trial
- Only cohort A included people with FGFR2 fusion/rearrangement ➔ cohort A used in appraisal

Population (Cohort A – people with FGFR2 translocation)	• Advanced/metastatic or surgically unresectable cholangiocarcinoma which has not responded to previous therapy ○ Predominantly (98%) intra-hepatic cholangiocarcinoma. • Radiographically measurable or evaluable disease per RECIST v1.1 • Tumour assessment for FGF/FGFR gene alteration status • ECOG PS 0–2 • Life expectancy ≥ 12 weeks	
Locations	120 sites in 12 countries (9 sites in UK)	
Demographics	**Cohort A**	
	N	108
	Region – Western Europe	30%
Intervention	Pemigatinib, orally once daily for 2 weeks then 1 week off	
Follow up	Median: [redacted]	
ORR (95% CI)	Median: [redacted]	
PFS (95% CI) - months	Median: [redacted]	
OS (95% CI) - months	Median: [redacted]	
% on treatment at 2 yrs	[redacted]	

CI: Confidence interval; ECOG PS; Eastern cooperative oncology group performance status; ORR: Objective response rate; OS: Overall survival; PFS: Progression-free survival

Comparative evidence – Summary

- No head to head randomised trials comparing pemigatinib with SoC
- Comparator evidence from ABC-06 randomised phase 3, multi-centre, open-label study:
  - active symptom control (ASC) alone or modified folinic acid, 5-fluorouracil and oxaliplatin chemotherapy with ASC (mFOLFOX+ASC)
  - people with locally advanced/metastatic **biliary tract cancers** previously-treated with cisplatin/gemcitabine chemotherapy
  - UK only study: N=81 for ASC alone arm, N=81 for mFOLFOX+ASC arm
- As there is no direct comparative evidence pemigatinib is compared with ASC alone and with mFOLFOX+ASC using matching adjusted indirect comparison (MAIC)

Patient characteristics at baseline for studies considered for MAIC analysis

Study	FIGHT-202 (Cohort A)*	ABC-06	
Treatment	**Pemigatinib**	**ASC**	**mFOLFOX+ASC**
N	107	81	81
FGFR2+, N (%)	107 (100)	NR	NR
Median age: years (range)	56 (26–77)	65 (26–81)	65 (26–84)
Men, N (%)	42 (39)	37 (46)	43 (53)
Intrahepatic CCA, N (%)	105 (98)	38	34
ECOG PS: 0–1, N (%)	102 (95)	81 (100)	81(100)
Albumin: <35 g/L, N (%)	21 (20)	21 (26)	19 (23)

* One additional person was included from April 2020 data cut.
ASC: Active symptom control; ECOG: Eastern Cooperative Oncology Group; FGFR2: fibroblast growth factor receptor 2; mFOLFOX: oxaliplatin, L-folinic acid and fluorouracil; NR: not reported; PS: performance status

Source: adapted from company submission Table 16 (March 2019 data cut).

Comparative evidence – Results

MAIC results (FIGHT-202 data cut-off, 07 April 2020):

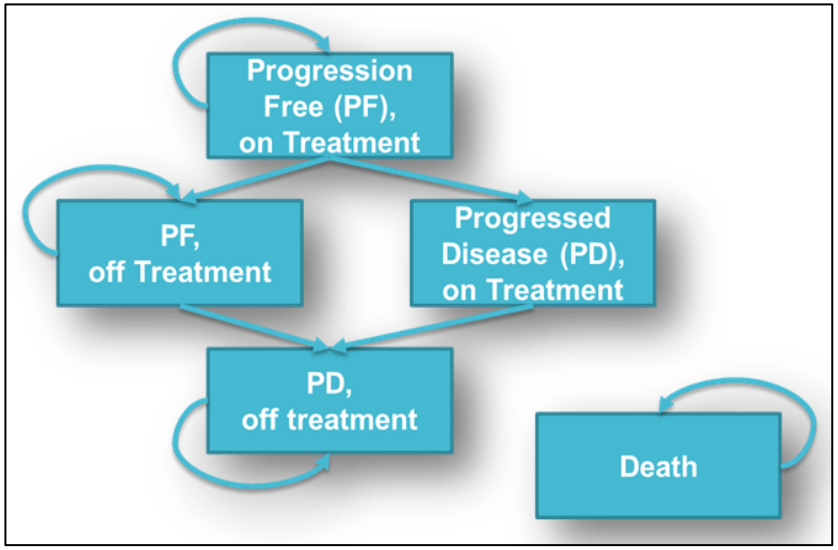
Pemigatinib versus	OS HR (95% CI):	PFS HR (95% CI):
mFOLFOX + ASC	Unadjusted = [redacted] Weighted† = [redacted]	Unadjusted = [redacted] Weighted† = [redacted]
ASC alone	Unadjusted = [redacted] Weighted† = [redacted]	K-M plot for PFS not available for ASC alone*

ASC: Active symptom control; CI: Confidence interval; HR: Hazard ratio; K-M: Kaplan Meier; mFOLFOX: Oxaliplatin, L-folinic acid and fluorouracil; OS: Overall survival; PFS: Progression-free survival

*PFS for ASC arm from ABC-06 was assumed to be equal to that of the mFOLFOX+ASC arm.
† Weighted OS and PFS HRs used in company's model. Weights are derived using a propensity score logistic regression model that uses individual patient data for the pemigatinib trial and published aggregate data from the comparator trial and estimates were obtained using the method of moments. OS and PFS were then compared between treatment groups using a weighted Cox proportional hazards model incorporating the weights from the propensity score model.

Economic model

- Partitioned survival model
- 40-year time horizon (life time)
- 1-week cycle length
- Costs and benefits discounted at 3.5% annually



Source: Company submission Document B, Figure 18.

Parameter	Pemigatinib	mFOLFOX+ASC,	ASC alone
Overall survival	FIGHT-202	HRs from MAIC applied to pemigatinib	
PFS	FIGHT-202	HRs from MAIC applied to pemigatinib*	
Time on treatment	FIGHT-202	equivalent to PFS, (mFOLFOX was limited to a maximum of 24 weeks)	equivalent to PFS
Adverse events (AEs)	FIGHT-202	Lamarca et al.2019	
HRQoL/utility	EORTC-QLQ-C30 data from FIGHT-202 mapped to EQ-5D utilities using Longworth et al., 2014 mapping algorithm		
Dosing	FIGHT-202	Lamarca et al.2019	
Other resource use	Clinical experts		
Costs	Drug prices: eMC; drug admin & AEs: NHS Reference costs; end of life: Round et al (2015); Multi-gene NGS test: clinical advice		

* PFS for ASC arm from ABC-06 was assumed to be equal to that of the mFOLFOX+ASC arm.
AEs: Adverse events; ASC: Active symptom control; eMC: electronic medicines compendium; EORTC-QLQ-C30; European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; HRQoL: Health related quality of life; MAIC: Matching adjusted indirect comparison; NGS: Next generation sequencing

Issues resolved after technical engagement

	Summary	ERG critique	Technical engagement responses	Base case
7	Company submission includes mFOLFOX+ASC) and ASC alone as comparators to pemigatinib.	Likely that other chemotherapy agents are also used in NHS ➔uncertainty in clinical guidelines and some clinical advice to company indicated preference for CAPOX over mFOLFOX.	Clinical experts advised that relevant comparators in routine clinical practice include mFOLFOX+ASC and ASC alone. ERG considers in light of clinical validation, mFOLFOX+ASC and ASC alone likely reflect standard practice.	Company ✓ ERG ✓
9	Company used exponential curve to extrapolate time on treatment in base case.	Weibull curve more closely matches clinical expert opinion.	Company revised it's base case to use Weibull distribution ➔preferred by the ERG due to the similarity between extrapolations and their visual and statistical fit and its proximity to estimates from clinical opinion.	Company ✓ ERG ✓

ASC: Active symptom control; CAPOX: oxaliplatin in combination with capecitabine

Issues resolved after technical engagement

	Summary	ERG critique	Technical engagement responses	Base case
11	When mapping EORTC-QLQ-C30 data from FIGHT-202 to EQ-5D-3L, company used regression model 5 with coefficients for treatment and progression status and interaction between these to generate health state utilities in its base case.	Regression model 5 results in lower utilities with PFS off treatment than with progressed disease ➔ ERG prefers regression model 3 with covariates for baseline utility and progression status only.	Company revised it's base case using regression model 3 to obtain health state utilities.	Company ✓ ERG ✓
12 a	Drug wastage not included in company submission.	Justifiable for chemotherapy given lower acquisition costs. For pemigatinib, as dose reductions may occur, the ERG prefers to include drug wastage for pemigatinib.	Company updated base case to include wastage for pemigatinib.	Company ✓ ERG ✓

Issues unresolved post technical engagement

Key issues unresolved post technical engagement	Status	Impact	Slide
Issue 2: Efficacy of pemigatinib is for a subset of the specified population • Is the population from FIGHT-202 reflective of NICE scope and people who would be offered pemigatinib in NHS clinical practice?	**To discuss**		15
Issue 1, 3, 4, 5 & 10: Comparative evidence • Is the comparative evidence to estimate relative efficacy of pemigatinib appropriate? • Is the population from ABC-06 reflective of population in FIGHT-202 and NICE scope? • Are the results of MAIC analysis reliable? • Is it appropriate to use unadjusted AEs rates in the model?	**To discuss**		16-17
Issue 8: Selection of pemigatinib OS curve • Which parametric curve should be used to model long-term OS?	**To discuss**		18-19
Issue 12b: Genetic testing costs • Should the genetic testing cost provided by NHS England be included in the model?	**To discuss**		20-21
Issue 6: End of life criteria • Does pemigatinib meet NICE EoL criteria?	**To discuss**	N/A	22-23

Key:
 Model driver;  Unknown impact;  Small/moderate impact

Issue 2: Efficacy of pemigatinib is for a subset of the specified population

Background

- NICE final scope population is defined as advanced CCA with FGFR2 fusion/rearrangement that is relapsed or refractory after at least 1 prior systemic therapy.
- Company's trial evidence does not cover the full population in the NICE scope.

ERG comments

- FIGHT-202
  - 98% of the patients had iCCA.
  - Acknowledges approximately 95% patients with FGFR2 mutations, have iCCA.
- Advanced Biliary Tract Cancer trials conducted in the UK suggest that iCCAs account for around 34% of CCA cases.

Clinical expert comments:

- To be eligible for pemigatinib, patients will be identified by the presence of the molecular alteration (FGFR2 fusion) and not by subtype of CCA.
- FGFR2 fusion could also be identified in non-intrahepatic CCA.
- In the advanced setting it is difficult to differentiate iCCA from other subtypes.

Company comments:

- No biological rationale that pemigatinib would not provide benefit to non-iCCA patients with FGFR2 fusion/rearrangements.

Is the population from FIGHT-202 reflective of NICE scope and people who would be offered pemigatinib in NHS clinical practice?

Issues 1, 3, 4, 5 & 10: Comparative evidence

Background

Issue 1:

- No direct comparative evidence for the efficacy and safety of pemigatinib versus comparators.

Issue 3:

- Lack of evidence of efficacy and safety of the comparators in the specified population
- ABC-06 population does not match population in FIGHT-202 and NICE scope.

Issue 4:

- Estimate of relative treatment effect of pemigatinib versus mFOLFOX+ASC and ASC was based on an unanchored MAIC.
- High level of uncertainty introduced by MAIC based on mismatched trials

Issue 5 & 10:

- Lack of evidence of comparative safety of pemigatinib versus comparators
- No MAIC analysis conducted for adverse events (AEs) ➔ Used unadjusted AEs data

Company comments

- Uncertainty from the lack of direct comparative efficacy evidence linked to disease rarity.
- ABC-06 reflects best available comparator evidence; it was used to formulate UK treatment guidance ➔ alternative comparator studies subject to same unresolvable uncertainties.
- MAIC performed following NICE TSD18 ➔ updated using FIGHT-202 data from April 2020.
- No MAIC analysis for AEs due to lack of available evidence ➔sensitivity analysis shows cost-effectiveness estimates are insensitive to comparative safety data.
- FIGHT 302 is expected to provide comparative evidence in untreated patients

Issues 1, 3, 4, 5 & 10: Comparative evidence

Clinical expert comments

- CCA is a rare cancer ➔ difficult to undertake comparative studies in sub-populations.
- A clinical expert suggested MAIC analysis for AEs should be considered.

Stakeholder comments

- Data presented are consistent with similar drugs undergoing evaluation in clinical studies
- Analysis of efficacy or safety in FGFR2 fusion population from ABC-06 have yet to be done.
- FGFR2 fusion patients would not behave any differently to non-FGFR2 fusion patients.

ERG critique:

- Estimate of comparative treatment effect and the ICERs uncertain and likely to be biased.
- Issues are unresolvable with current evidence.
- No conclusions can be drawn about the safety profile of pemigatinib, relative to second-line systemic chemotherapy regimens, in the specified population.
- Little impact of AEs on cost-effectiveness results ➔ Direction of impact unknown.
- Little value in performing a MAIC on AEs ➔ MAIC analysis of weak quality.
- FIGHT-302 in untreated patients will not resolve uncertainty in previously treated patients.

Can the available comparative evidence be used for decision making?

- Is the comparative evidence to estimate relative efficacy of pemigatinib appropriate?
- Is the population from ABC-06 reflective NICE scope and patients seen in NHS?
- Are the results of MAIC analysis reliable?
- Is it appropriate to use unadjusted AEs rates in the economic modelling?

Issue 8: Selection of pemigatinib OS extrapolation

Background

- Company fitted log-logistic curve to pemigatinib OS K-M data from FIGHT-202 (March 2019 data cut).
  - Clinical advice to company suggested 5% survival with pemigatinib at five years.
  - Literature sources report estimated 5-year survival rate with pemigatinib of ≤10%.
- **ERG:** preferred to model long term pemigatinib survival using generalised gamma (March 2019 data cut)
  - 3% survival with pemigatinib at 5-years estimated using generalised gamma curve provides the closest estimate to clinical expert advice
  - little difference between generalised gamma and log-logistic statistical fit.
- Pemigatinib OS considered a key model driver with significant impact on ICER.

Company's response to technical engagement:

- Updated pemigatinib OS data and survival analysis provided using additional follow-up from April 2020 data cut ➔ reduces uncertainty of long-term survival outcomes.
- Clinical validation supports use of the log-logistic distribution in the base case analysis.
  - predicts a declining predicted hazard over time consistent with the published literature.
- Prefers log-logistic curve to extrapolate pemigatinib OS estimate.

ERG critique:

- Additional evidence does not narrow down extrapolations to a more plausible selection.
- The estimate of 5% survival at 5-years for patients receiving pemigatinib remains the only long-term estimate of clinical validity.
- Still prefers generalised gamma.

Issue 8: Selection of pemigatinib OS extrapolation

OS K-M data and parametric survival models for pemigatinib (FIGHT-202, April 2020 data) and mFOLFOX+ASC and ASC alone (ABC-06)

Pemigatinib 5-year survival (April 2020 data)

Model	5-year survival estimates
Exponential	[redacted]
Generalised gamma	[redacted]
Gompertz	[redacted]
Log-logistic	[redacted]
Log-normal	[redacted]
Weibull	[redacted]

Source: Pemigatinib Incyte TE CE model ERG BC new PAS v1.0 08042021

Which extrapolation is most appropriate to model long-term OS?

Issue 12b: Costs for genetic testing

Background

- The company did not include FGFR genetic testing costs in their base case analysis.
  - Included scenario analysis with FGFR genetic testing costs.
- Scenario assumed testing costs of £6,395 per additional FGFR2-fusion positive patient based on company's clinical consultation.
- **ERG:** Does not agree with the exclusion of genetic testing costs.

Clinical expert comments:

- Genomic testing is not performed as routine clinical practice in UK.
- Analysis of cost and efficacy needs to include genomic testing for the whole population.
- Tests would be indicated in all CCA patients.
- Cost of the genetic testing depends on the technology used and the potential additional. need to have another tissue biopsy.

Company comments:

- Genetic testing is not specific to the identification of FGFR2 ➔ not included in base case.
- It is already being carried out in the NHS for CCA patients to identify the presence of NTRK rearrangements ➔ process is likely to become routine clinical practice

ERG critique:

- For patients with CCA, the 2020/21 National Genomic Test Directory (NGTD) does not include testing for FGF/FGFR gene alterations.
  - NGTD indicates some tests that are listed may not yet be available.
- ERG identified different assumptions for unit costs of testing and prevalence of FGFR2

Issue 12b: Costs for genetic testing

Alternative assumptions for the unit cost of NGS genetic testing and prevalence of FGFR2 fusions:

Source	Unit cost	Prevalence	Cost per eligible patient
Cost: company consultation with several providers including NHS laboratories, taking into consideration factors specific to the processing of CCA samples **Prevalence:** Hollebecque et al., 2019	£550	8.6%	£6,395
Additional costs identified by ERG **Cost:** Schwarze et al., 2020 **Prevalence:** Hollebecque et al., 2019	£6,841	8.6%	£79,547

NHS England comments:

- Genetic testing costs to be included in the cost-effectiveness analysis
- Costs of gene panel testing have been provided to the Genomic Laboratory Hubs for such testing by NHS England ➔ Cost in this appraisal should be incremental to the gene panel
- Cost of adding the FGFR2 test to the current solid tumour panel is £34.
- One FGFR2 genomic change requires 10 tests - 10% prevalence.
  - incremental cost of testing should be £340 per eligible patient.

Should the genetic testing cost provided by NHS England be included in the model?

Issue 6: End of life criteria

Background

- Based on the economic model, company considers pemigatinib meets end of life (EoL) criteria

ERG comments

- ERG base case suggests pemigatinib meets EoL criteria.
- Given uncertainty in clinical inputs, it is not clear if pemigatinib meets EoL criteria
  - data not mature at 22nd March 2019 cut-off
  - high level of uncertainty with MAIC
  - outcomes of people with advanced CCA with FGFR2 fusion or rearrangement treated with second-line systemic chemotherapy are uncertain

Company comments

- Analysis provided with updated April 2020 data cut
- Tested existing modelling assumptions using extreme values of OS HR.
  - HR estimates (for wild-type patients versus FGFR2 fusions) varied between 0.2 and 4
  - the mean total life years for comparators never rose above 24 months
  - mean incremental life year gains for pemigatinib versus mFOLFOX+ASC fell to a minimum value of 7.64 months
- Clinical validation indicates pemigatinib clearly meets NICE EoL criteria, despite uncertainty in comparative efficacy between pemigatinib and comparators

Issue 6: End of life criteria

Criterion	Comparator	Company's base case†	ERGs base case#
		Mean life expectancy (months) - undiscounted*	
Short life expectancy: normally < 24 months	mFOLFOX+ASC	8.02	8.00
	ASC alone	7.28	7.26
	Pemigatinib comparison	Mean incremental life expectancy (months)- undiscounted*	
Extension to life: normally ≥ 3 months	vs mFOLFOX+ASC	25.63	19.40
	vs ASC alone	26.38	20.15

*Calculated by NICE technical team; †Assumes loglogistic OS extrapolation; #Assumes generalised gamma OS extrapolation

- FIGHT-202 pemigatinib median OS of [redacted] months (April 2020 data cut).

Clinical expert comments

- Chemorefractory CCA patients in absence of FGFR2-targeted therapy have a life expectancy ranging between 4.7 to 10 months.
- Another expert said expected survival is around 6 months

Stakeholder comments

- Median OS from ABC-06 and FIGHT-202 are difficult to interpret because they include patients at different stages of disease.

ERG critique

- Substantial unquantified uncertainties in the comparison of mismatched populations

Does pemigatinib meet NICE EoL criteria in the specified population for this appraisal?

Innovation and equality

Innovation

- Company submission highlights that pemigatinib addresses the urgent unmet need in people with advanced or metastatic CCA harbouring an FGFR2 fusion/rearrangement who have progressed on at least one line of prior therapy in England.
  - No approved targeted therapy in these people ➔ Salvage chemotherapy regimens have shown variable efficacy and systemic toxicity.

- During technical engagement, a clinical expert suggested pemigatinib would make a significant impact on health-related benefits for these patients by improving their quality of life and extending their life expectancy.

Equality

- During technical engagement, a clinical expert highlighted the need for molecular testing being available to cholangiocarcinoma population

- **Is pemigatinib an innovative treatment for relapsed or refractory advanced cholangiocarcinoma with FGFR2 alterations?**
- **Are there any additional benefits with pemigatinib that have not been captured adequately in the economic model?**
- **Are there any equality issues relevant to this appraisal?**

Cost-effectiveness results: Company's base case

(April 2020 data cut)

Key assumptions:

- Extrapolation of pemigatinib OS estimate ➔ Log-logistic
- Extrapolation of pemigatinib PFS estimate ➔ Log-normal*
- Extrapolation of pemigatinib ToT estimate ➔ Weibull*
- PFS for ASC arm from ABC-06 ➔ Equal to PFS for mFOLFOX+ASC arm*
- Estimate of health state utility values ➔ regression model 3 excluding treatment status*
- Wastage costs included*
- Exclusion of genetic testing costs for pemigatinib

Company's base-case fully incremental deterministic results (PAS price)

Technology	Total Costs (£)	Total QALYs	Incr. costs (£)	Incr. QALYs	ICER (£/QALY)
ASC alone	[redacted]	[redacted]	-	-	-
mFOLFOX+ASC	[redacted]	[redacted]	[redacted]	[redacted]	154,493 / Extendedly dominated†
Pemigatinib	[redacted]	[redacted]	[redacted]	[redacted]	51,952

Company's base-case pairwise deterministic results versus mFOLFOX+ASC (PAS price)

Technology	Incr. costs (£)	Incr. QALYs	ICER (£/QALY)
mFOLFOX+ASC	-	-	-
Pemigatinib	[redacted]	[redacted]	49,186

*Included in ERG base case

†mFOLFOX+ASC is less effective and has a higher ICER than pemigatinib versus ASC alone

Cost-effectiveness results: ERG's base case (April 2020 data cut)

Key variations from company's base case assumptions:

- Extrapolation of pemigatinib OS estimate ➔ Generalised gamma
- Inclusion of genetic testing costs for pemigatinib – £550 based on company's clinical consultation

ERG's base-case fully incremental deterministic results (PAS price)

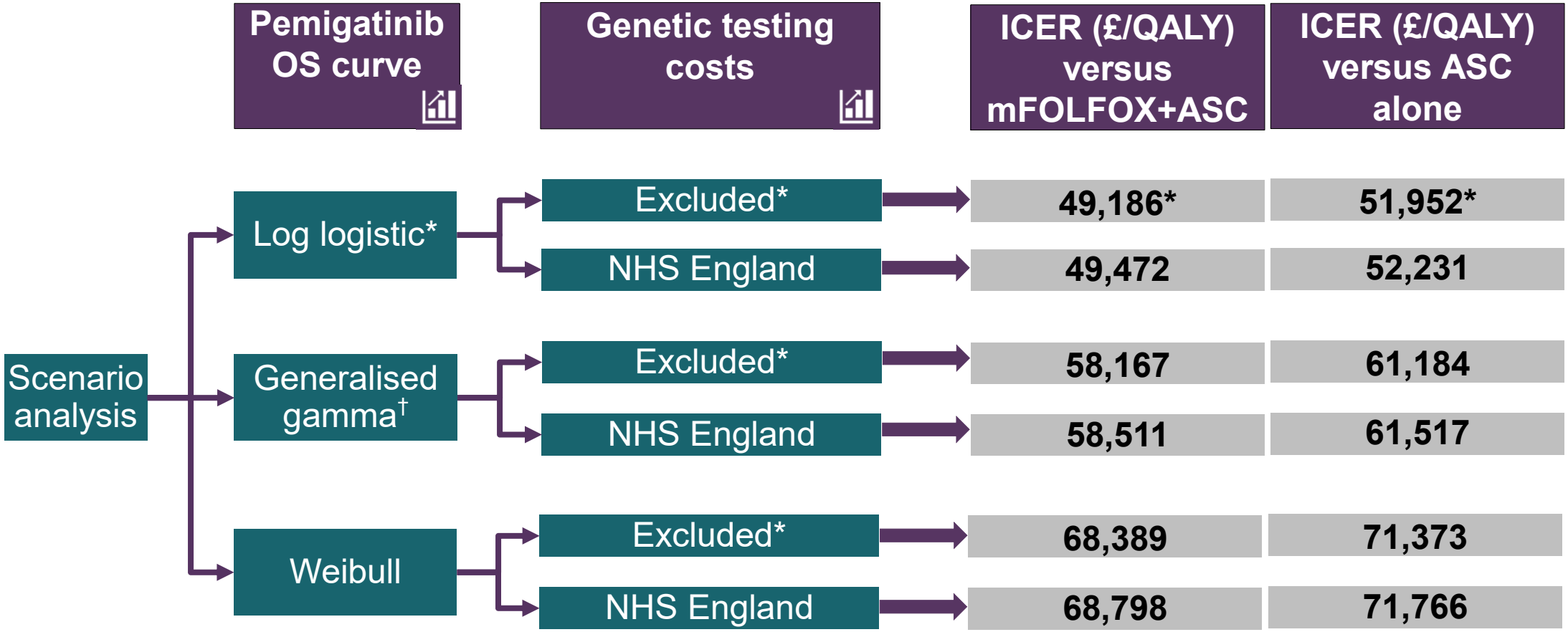
Technology	Total Costs (£)	Total QALYs	Incr. costs (£)	Incr. QALYs	ICER (£/QALY)
ASC alone	[redacted]	[redacted]	-	-	-
mFOLFOX+ASC	[redacted]	[redacted]	[redacted]	[redacted]	153,707 / Extendedly dominated
Pemigatinib	[redacted]	[redacted]	[redacted]	[redacted]	67,448

ERG's base-case fully incremental probabilistic results (PAS price)

Technology	Total Costs (£)	Total QALYs	Incr. costs (£)	Incr. QALYs	ICER (£/QALY)
ASC alone	[redacted]	[redacted]	-	-	-
mFOLFOX+ASC	[redacted]	[redacted]	[redacted]	[redacted]	147,786 / Extendedly dominated
Pemigatinib	[redacted]	[redacted]	[redacted]	[redacted]	63,122

Scenario analysis – PAS price

Deterministic results – NHS England genetic testing costs

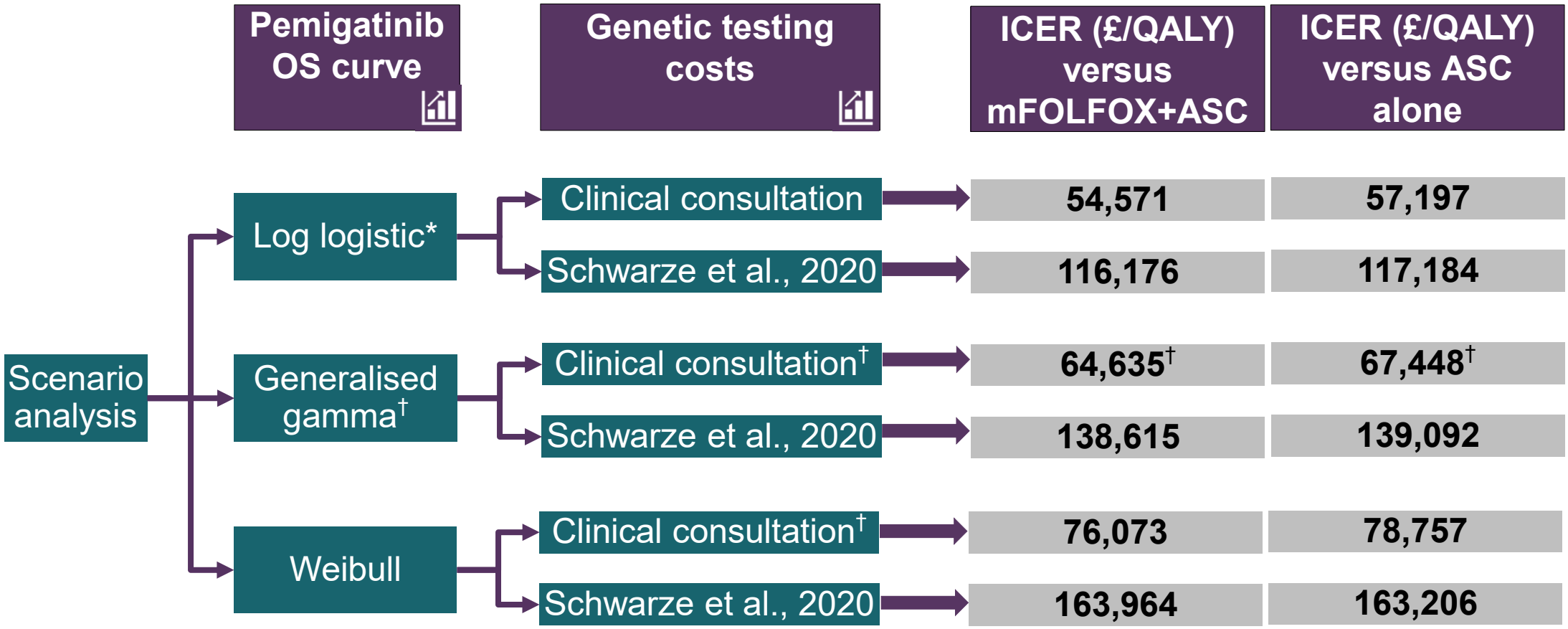


NHS England: £34 unit cost and 10% prevalence - £340 per FGFR2+ patient

* Company's preferred approach
† ERG's preferred approach

Scenario analysis – PAS price

Deterministic results – additional genetic testing scenarios



Clinical consultation: £550 unit cost and 8.6% prevalence - £6,395 per FGFR2+ patient
Schwarze et al., 2020: £6,841 unit cost and 8.6% prevalence- £79,547 per FGFR2+ patient

* Company's preferred approach
† ERG's preferred approach

NICE

Issues unresolved post technical engagement

Key issues unresolved post technical engagement	Status	Impact	Slide
Issue 2: Efficacy of pemigatinib is for a subset of the specified population • Is the population from FIGHT-202 reflective of NICE scope and people who would be offered pemigatinib in NHS clinical practice?	**To discuss**		15
Issue 1, 3, 4, 5 & 10: Comparative evidence • Is the comparative evidence to estimate relative efficacy of pemigatinib appropriate? • Is the population from ABC-06 reflective of population in FIGHT-202 and NICE scope? • Are the results of MAIC analysis reliable? • Is it appropriate to use unadjusted AEs rates in the model?	**To discuss**		16-17
Issue 8: Selection of pemigatinib OS curve • Which parametric curve should be used to model long-term OS?	**To discuss**		18-19
Issue 12b: Genetic testing costs • Should the genetic testing cost provided by NHS England be included in the model	**To discuss**		20-21
Issue 6: End of life criteria • Does pemigatinib meet NICE EoL criteria?	**To discuss**	N/A	22-23

Key:
 Model driver;  Unknown impact;  Small/moderate impact