NICE National Institute for Health and Care Excellence

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

Chair's presentation

Chair: Stephen O'Brien

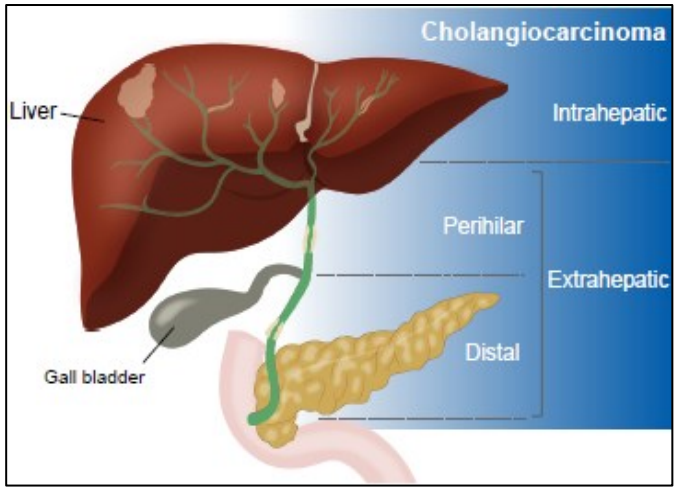
ERG: Kleijnen Systematic Reviews (KSR)

Technical team: Elizabeth Bell, Alexandra Filby, Ross Dent

Company: Incyte Biosciences UK

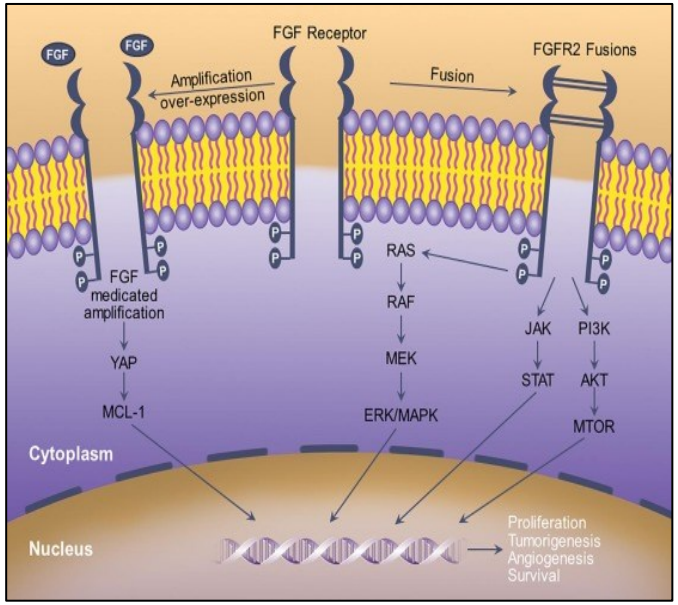
ACM2: 16 June 2021

Disease background



Cholangiocarcinoma (CCA)

- CCA is a rare cancer, with 2,187 people diagnosed with CCA in England in 2017
- 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
- CCA develops from the epithelial lining of the bile ducts.



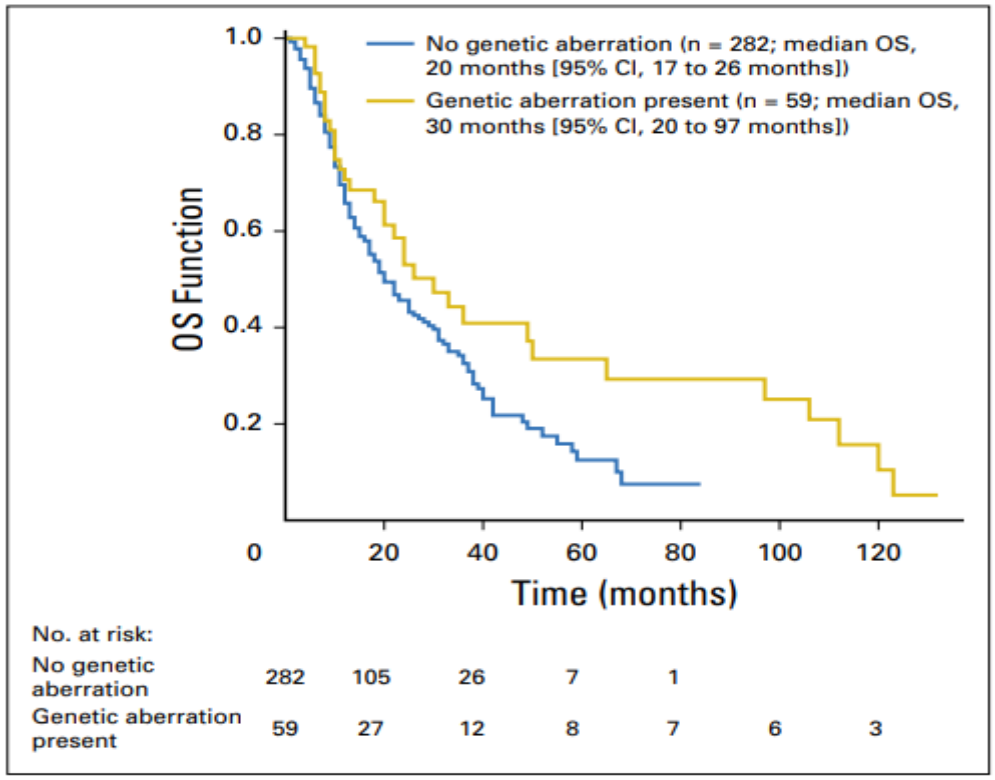
FGFR2 alterations

- 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 to 20% of all iCCA
- Standard of care (SoC) for locally advanced or metastatic CCA is chemotherapy with a gemcitabine-based doublet
  - SoC has a median overall survival (OS) of approximately 12 months.

CCA: Cholangiocarcinoma; eCCA: Extrahepatic CCA; FGFR: Fibroblast growth factor receptor; iCCA: Intrahepatic CCA; OS: Overall survival; SoC: Standard of Care

FGFR genetic aberrations* in CCA

OS curves split by with/without FGFR aberrations. n=36 excluded who had FGFR-directed therapy (P=0.02666). Jain *et al*.



*Genetic aberrations are: fusion, amplification or mutation of FGFR 2 (most common: 78%) as well as FGFR 1, 3, 4, 19

Baseline characteristics

	All patients	iCCA	eCCA	Gall bladder
	n=377 (100%)	n=273 (72%)	n=44 (12%)	n=60 (16%)
FGFR abnormal	95/377 (25%)	83/273 (30%)	4/44 (9%)	8/60 (13%)
FGFR normal	282/377 (75%)	190/273 (70%)	40/44 (91%)	52/60 (87%)

ERG comment on Jain *et al* study

- A retrospective analysis with a relatively small number of patients
- A reasonable set of potentially prognostic variables have been considered that were considered significant ($p<0.05$) in univariable analysis
- Full results of multivariable modeling are not reported.

Source: Jain A, et al. (2018) Cholangiocarcinoma With FGFR Genetic Aberrations: A Unique Clinical Phenotype. JCO Precision Oncology.
eCCA: Extrahepatic CCA; FGFR: Fibroblast growth factor receptor; iCCA: Intrahepatic CCA; OS: Overall survival

Pemigatinib (Pemazyre, Incyte Biosciences UK)

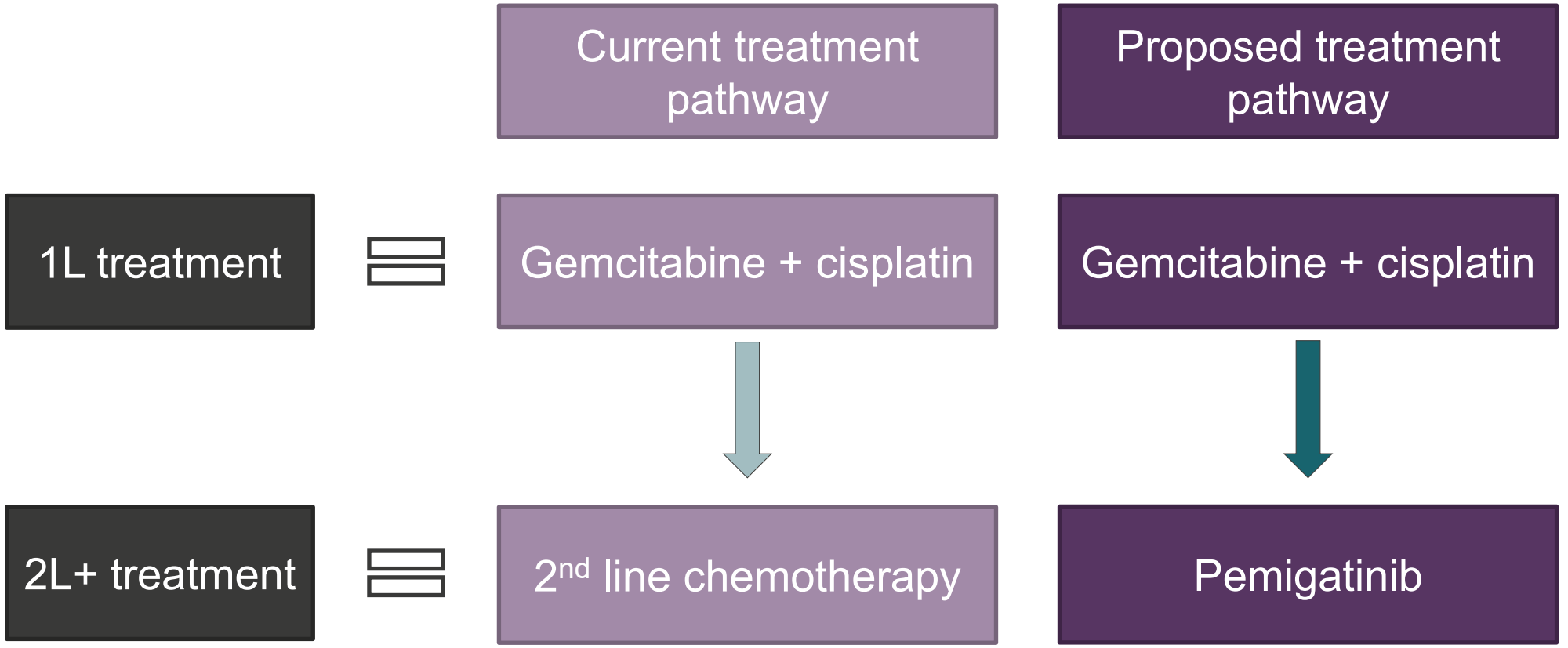
Mechanism of action	Pemigatinib is a potent and selective FGFR 1, 2, and 3 inhibitor. Pemigatinib blocks autophosphorylation and activation of major FGF/FGFR signalling pathways, inhibiting the growth of cells with FGFR2 fusions/rearrangements.
Conditional marketing authorisation	MA (MHRA): Treatment of adults with locally advanced or metastatic CCA with a FGFR2 fusion or rearrangement that have progressed after at least 1 prior line of systemic therapy.
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 (PAS). With the **updated PAS** the annual cost is estimated to be [redacted].

Conditional marketing authorisation can be granted if all 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.

CCA: Cholangiocarcinoma; FGF; Fibroblast growth factor; FGFR: Fibroblast growth factor receptor; PAS: Patient access scheme

Treatment pathway



1L: First line; 2L: Second line

Clinical evidence

Comparators	mFOLFOX+ASC and ASC alone		
Pemigatinib clinical trial	FIGHT-202 (cohort A). Single-arm, phase 2, open-label trial for advanced/metastatic or surgically unresectable CCA which has not responded to previous therapy (98% iCCA)		
mFOLFOX+ASC and ASC clinical trial	ABC-06. Open-label randomised phase 3 study of active symptom control (ASC) alone or mFOLFOX+ASC for people with locally advanced or metastatic biliary tract cancers previously treated with gemcitabine plus cisplatin chemotherapy		
Relative treatment: matched adjusted indirect comparison (MAIC) between FIGHT-202 and ABC-06	**Pemigatinib versus**	**Overall survival Hazard Ratio (HR) (95% CI)**	**Progression-free survival HR (95% CI)**
	mFOLFOX+ ASC	Unadjusted = [redacted] Weighted = [redacted]	Unadjusted = [redacted] Weighted = [redacted]
	ASC alone	Unadjusted = [redacted] Weighted = [redacted]	PFS for ASC arm from ABC-06 was assumed equal to that of the mFOLFOX+ASC arm

ASC: Active symptom control; CCA: Cholangiocarcinoma; CI: Confidence interval; HR: Hazard ratio; iCCA: intrahepatic cholangiocarcinoma; MAIC: Matching adjusted indirect comparison; mFOLFOX: Modified oxaliplatin, L-folinic acid and fluorouracil; OS: Overall survival; PFS: Progression-free survival

ACD recommendation

ACD recommendation	• Pemigatinib is **not** recommended for treating locally advanced or metastatic CCA with FGFR2 fusion or rearrangement that has progressed after systemic therapy in adults

Summary of why the committee made these decisions	• Clinical evidence is highly uncertain
	  • The trial did not directly compare pemigatinib with symptom control or mFOLFOX
	  • Results of the indirect comparison are uncertain

Committee requested to see	• Clearer justification for the selected parametric curves for OS and independent models • Include the cost of FGFR2 testing and optical coherence tomography (OCT) costs

CCA: Cholangiocarcinoma; FGFR: Fibroblast growth factor receptor; mFOLFOX: Modified oxaliplatin, L-folinic acid and fluorouracil; OCT: Optical coherence tomography

RECAP

Committee's preferred assumptions resolved after ACM1

Issue	Committee preference	Company revised base case
Comparators	mFOLFOX+ASC and ASC alone are the most appropriate comparators for this appraisal	✓
Population	Cohort A of FIGHT-202 is appropriate for decision making	✓
MAIC results	Despite limitations, the comparative efficacy estimates from the MAIC using ABC-06 is appropriate for decision making	✓
Safety evidence	There is a lack of comparative safety evidence but this is likely to have little effect on the cost-effectiveness estimates	✓
End of life criteria	Pemigatinib is considered a life-extending treatment at the end of life	✓
Genetic testing	NHS England's genetic testing costs and the prevalence of FGFR2 fusion or rearrangement should be included in the cost-effectiveness analysis	✓
OCT	The costs of OCT should be included in the economic analysis	✓

Updated pemigatinib patient access scheme (PAS) submitted by the company

ASC: Active symptom control; MAIC: Matching adjusted indirect comparison; mFOLFOX: Modified oxaliplatin, L-folinic acid and fluorouracil

Comparator issues

ERG	Company	Committee's conclusion
No direct comparative evidence for the efficacy and safety of pemigatinib versus comparators.	The clinical evidence for pemigatinib came from cohort A of FIGHT-202, a single arm trial which included people with FGFR2 fusion or rearrangement.	Indirect comparisons were needed to assess the relative effectiveness of pemigatinib compared with the comparators.
The estimate of comparative treatment effect is highly uncertain and likely to be biased, because the MAIC was done between mismatched trial populations.	The weightings in the MAIC were derived using a propensity score logistic regression model adjusted for selected prognostic factors. In general, the results were more favourable for pemigatinib.	The MAIC suggests pemigatinib is likely to be more effective than the comparators.

Committee conclusion: comparative evidence has limitations but is the best available evidence and is appropriate for decision making

MAIC: Matching adjusted indirect comparison

End of life criteria

Recap	Committee's conclusion
Company - base case model estimated: • Mean undiscounted life expectancy of 8.0 months and 7.3 months for mFOLFOX+ASC and ASC alone, respectively • Mean undiscounted extension to life with pemigatinib of 25.6 months and 26.4 months compared with mFOLFOX+ASC and ASC alone, respectively. ERG • Life-extension estimates are highly uncertain given the uncertainty in the results from the MAIC and the approach used to estimate health outcomes in the model. Clinical experts • People with relapsed or refractory CCA with FGFR2 fusion or rearrangement have a life expectancy of between 4.7 and 10 months with current treatment.	• Short life expectancy criterion met • Extension to life criterion less certain because of limitations in survival analysis ○ However, risk of extension to life criterion not being met is relatively small, given estimates are substantially greater than 3 months.

Committee conclusion: pemigatinib is a life-extending treatment at the end of life.

ASC: Active symptom control; CCA: Cholangiocarcinoma; FGFR: Fibroblast growth factor receptor; MAIC: Matching adjusted indirect comparison; mFOLFOX: Oxaliplatin, L-folinic acid and fluorouracil

Consultation comments

Patient group and patient expert comments

People with CCA, eligible for pemigatinib, have high unmet need	Pemigatinib is effective	Pemigatinib may cost the NHS less than other cancers	Treatments for rare diseases should be considered
• Frequently diagnosed at a late stage • For people with inoperable CCA survival is limited • Recurrence is still possible after liver resection • Second line therapy does not always work and has stressful side effects.	• Pemigatinib has more manageable toxicities allowing people to continue with their normal activities • The use of targeted therapies in CCA represents the most valuable advance in the management of CCA in the last decade.	• There is so little in the way of treatments available to CCA patients • Survival in people with inoperable cancer is limited.	• People with rare diseases should be offered the right to a treatment which has proven success in prolonging life • Lack of significant data due to small population size should not discriminate the results • Other health authorities have already approved this treatment due to its success.

CCA: Cholangiocarcinoma

Key issues for consideration

Committee preference	
Overall survival	
1. Fitting independent models to each group is more appropriate	
2. Clinical expectations of survival in both groups at 3 and 5 years	
3. Justification of the selection of independent parametric survival models for overall survival in both groups	
4. Consideration of the empirical hazard function for OS over time and whether the selected model is consistent with this and the assessment of statistical fits	
5. Relevant external data to estimate expected survival for the comparator group	

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

OCT: Optical coherence tomography; OS: Overall survival

ACM1: Committee considerations of key issues

Issue	Brief recap	Committee's conclusion
Independent models	Company: • Applied the hazard ratio to the treatment arm to generate parametric curves for comparator survival.	• Applying the hazard ratios from the indirect • comparison requires the assumption of proportional hazards • The company's selected log-logistic parametric curve is not a proportional-hazards curve • More appropriate to fit independent models to the treatment and comparator arms.

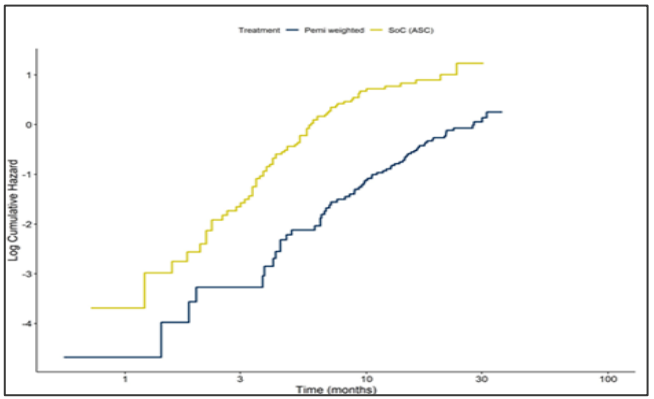
ACD consultation comments (company)

1. Analysis fitting independent models to treatment and comparator

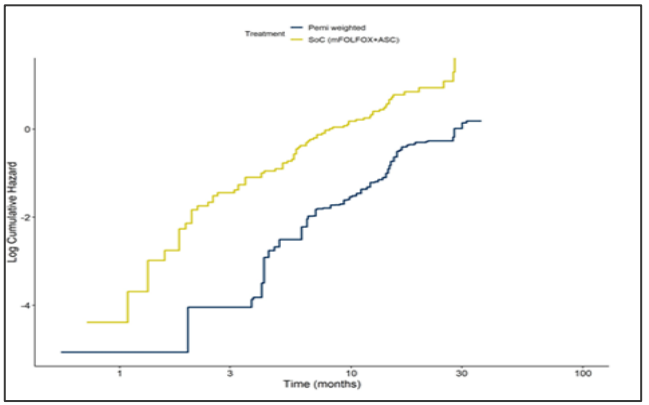
Company comment

- Company still use MAIC HR in base case:
  - The proportional hazards assumption does hold, so using a HR to generate comparator survival is appropriate
- Company still apply HR to accelerated failure time (AFT) model (log-logistic). Justified by doing a scenario using an appropriate model (exponential) → gave similar ICERs
- Independent models do not provide more robust or clinically plausible outcomes but this is provided as scenario analyses.

Log-cumulative hazard plots for MAIC adjusted pemigatinib overall survival versus ASC



Log-cumulative hazard plots for MAIC adjusted pemigatinib overall survival versus mFOLFOX+ASC



ERG comment

- Agree proportional hazards assumption is met
- But agree with committee that fitting independent curves to each arm is more appropriate

Should independent curves be fitted to each arm?

AFT: Accelerated failure time; ASC: Active symptom control; HR: Hazard ratio; ICER: Incremental-cost effectiveness ratio; MAIC: Matching adjusted indirect comparison; mFOLFOX: Modified oxaliplatin, L-folinic acid and fluorouracil; OS: Overall survival

ACM1: Committee considerations of key issues

Issue	Brief recap	Committee's conclusion

• Long-term survival estimates are unclear	Company:
	• The company's clinical expert suggested a 5% probability of OS at 5 years but struggled to choose the most plausible curve for the pemigatinib survival extrapolation
	  ○ Literature sources reported an estimated 5-year probability of less than 10%.
	Clinical experts:
	• Advised that 5% survival with pemigatinib is based on historical data
	• Would expect to see a 5-year survival with pemigatinib of about 10%.
		• There is a lack of clinical validation for the comparator arm
		  ○ A recent updated publication of ABC-06 may be informative
		• Clinical expectations of survival in both groups at 3 and 5 years and any relevant external data to estimate expected survival for the comparator group will be useful.

MAIC: Matching adjusted indirect comparison; OS: Overall survival

ACD consultation comments (company)

2. Additional clinical estimates of OS in both groups at 3 and 5 year

Company comment:

- Clinical validation comparator:
  - Patients receiving ASC alone
    - It would be unlikely for patients to survive beyond 3 years and therefore 5 years
  - Patients receiving mFOLFOX+ASC:
    - 3 years would be approximately 3%, while at 5 years this may be slightly higher than the 0.1% predicted in the original company base case.
- Clinical validation pemigatinib:
  - Based on evidence at the maximum follow-up of 3 years from FIGHT-202:
    - Predicted survival at 5 years would be between 10 to 13%.

ERG comment

- Estimate of 10 to 13% aligns with clinical estimates at ACM1 of 10% so prefers the lower end of the range.

ASC: Active symptom control; mFOLFOX: Modified oxaliplatin, L-folinic acid and fluorouracil; OS: Overall survival

ACM1: Committee considerations of key issues

Issue	Brief recap	Committee's conclusion
Justification for the preferred parametric curve	Company: • The company preferred the log-logistic curve to extrapolate survival with pemigatinib. ERG: • Preferred the generalised gamma model for extrapolation of survival with pemigatinib ○ This predicted a lower proportion of people would be alive at 5-years than the company's log-logistic model.	• The Weibull model gave the closest estimate to clinical opinion • The justification for the preferred parametric curve was unclear.

ACD consultation comments (company)

3. Justification of the selection of independent parametric survival models for OS in pemigatinib (1)

Company comment

- A scenario has been explored in which FIGHT-202 data and ABC-06 data are extrapolated independently
- Irrespective of which arm is used for the MAIC, the **log-logistic arm** remains a good candidate for the base case choice for OS extrapolation of FIGHT-202 data
    - **Generalised gamma** is also explored in scenario analysis.

ERG comment

- Log-logistic and generalised gamma are plausible
- Weibull is a less suitable candidate.

Which is the most appropriate parametric curve?

MAIC: Matching adjusted indirect comparison; OS: Overall survival

ACD consultation comments (company)

3&4. Justification of the selection of independent models for OS in the comparator and empirical hazards (1)

Company comment

- NICE TSD 14:
  - When modelling treatment arms independently, the same extrapolation function should be used across treatment arms
- The **log-logistic** extrapolation is a strong statistical fit for both arms of ABC-06, and the published evidence showing decreasing probability of death over time would also apply to the comparator arm
  - This was selected as the base case for OS in both comparator arms
  - Generalised gamma is also explored in scenario analysis.

ERG comment

- Empirical hazards:
  - ASC: log-logistic, gen. gamma and log-normal fit well
  - mFOLFOX+ASC: none of the curves fit well but may be due to small patient numbers
- Parametric curves:
  - Log-normal and generalised gamma plausible for mFOLFOX+ASC and ASC.

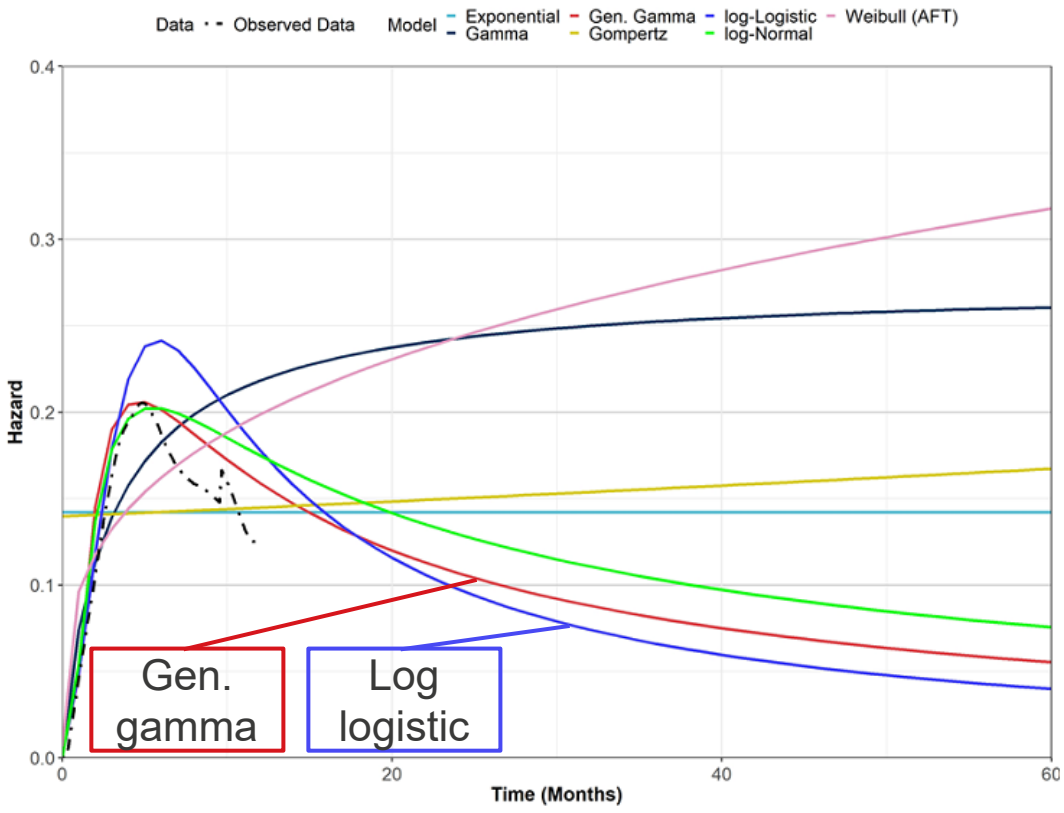
Which is the most appropriate parametric curve and is the selected model consistent with the observed empirical hazard function over time?

ASC: Active symptom control; HR: Hazard ratio; KM: Kaplan Meier; MAIC: Matching adjusted indirect comparison; mFOLFOX: Modified oxaliplatin, L-folinic acid and fluorouracil; OS: Overall survival

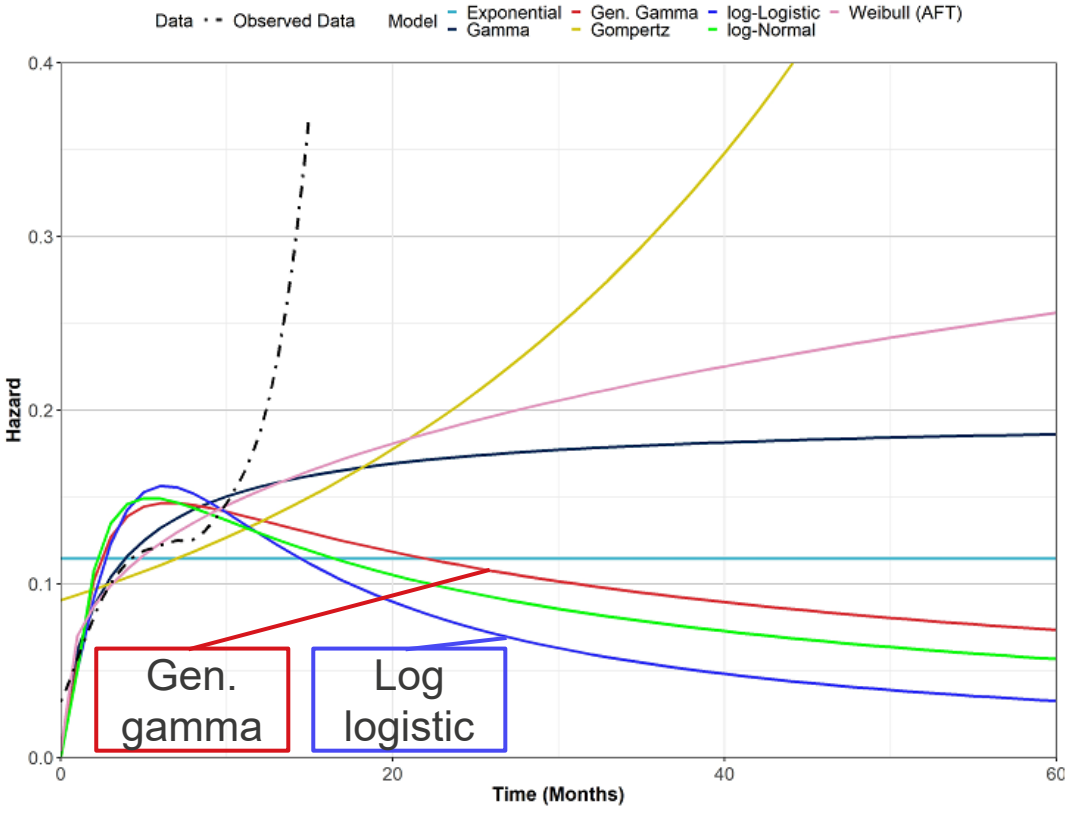
ACD consultation comments (company)

3&4. Justification of the selection of independent models for OS in the comparator and empirical hazards (2)

ABC-06 ASC, OS smoothed hazard plots



ABC-06 mFOLFOX, OS smoothed hazard plots



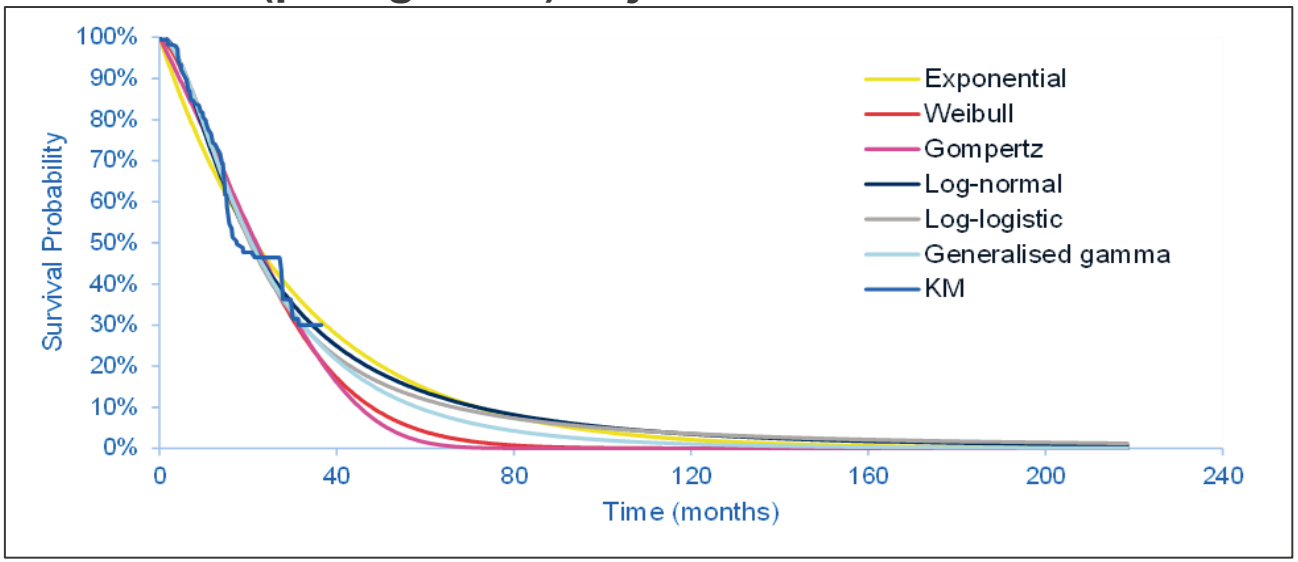
ASC: Active symptom control; mFOLFOX: Modified oxaliplatin, L-folinic acid and fluorouracil; OS: Overall survival

ACD consultation comments (company)

3. Justification of the selection of independent parametric survival models for OS in pemigatinib (2)

Company base case: log-logistic **Company scenario:** gen. gamma

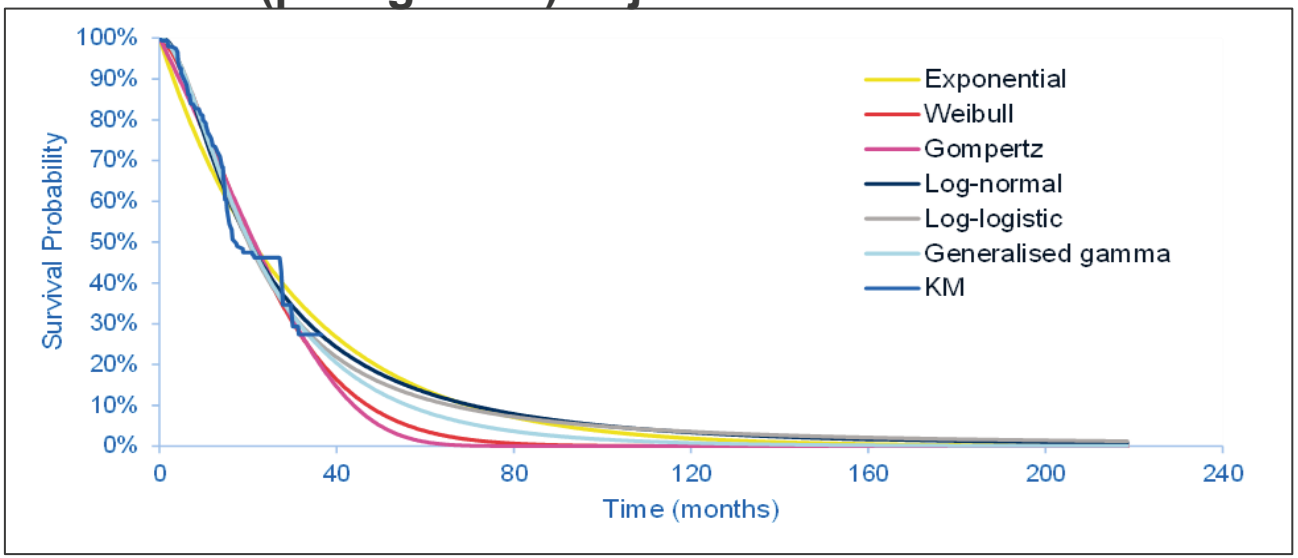
FIGHT-202 (pemigatinib) adjusted for ABC-06 mFOLFOX+ASC



Company expert: 5-year survival **10 to 13%**

Model	3-year OS	5-year OS
Exponential	31.4%	14.6%
Gen. gamma	25.5%	9.3%
Gompertz	21.9%	1.5%
Log-logistic	25.8%	11.9%
Log-normal	28.4%	13.6%
Weibull	22.0%	4.0%

FIGHT-202 (pemigatinib) adjusted for ABC-06 ASC



Model	3-year OS	5-year OS
Exponential	30.3%	13.8%
Gen. gamma	24.3%	8.4%
Gompertz	20.3%	1.0%
Log-logistic	25.2%	11.6%
Log-normal	27.6%	13.2%
Weibull	21.0%	3.7%

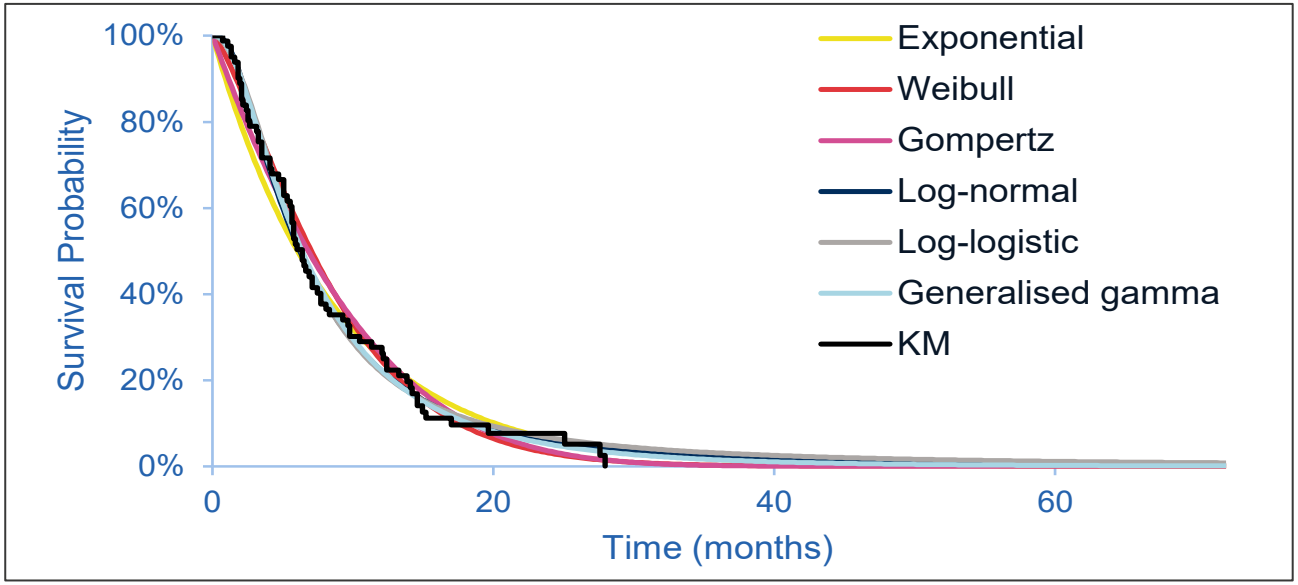
ASC: Active symptom control; mFOLFOX: Modified oxaliplatin, L-folinic acid and fluorouracil; OS: Overall survival

ACD consultation comments (company)

3. Justification of the selection of independent models for OS in the comparator (3)

Company base case: log-logistic **Company scenario:** gen. gamma

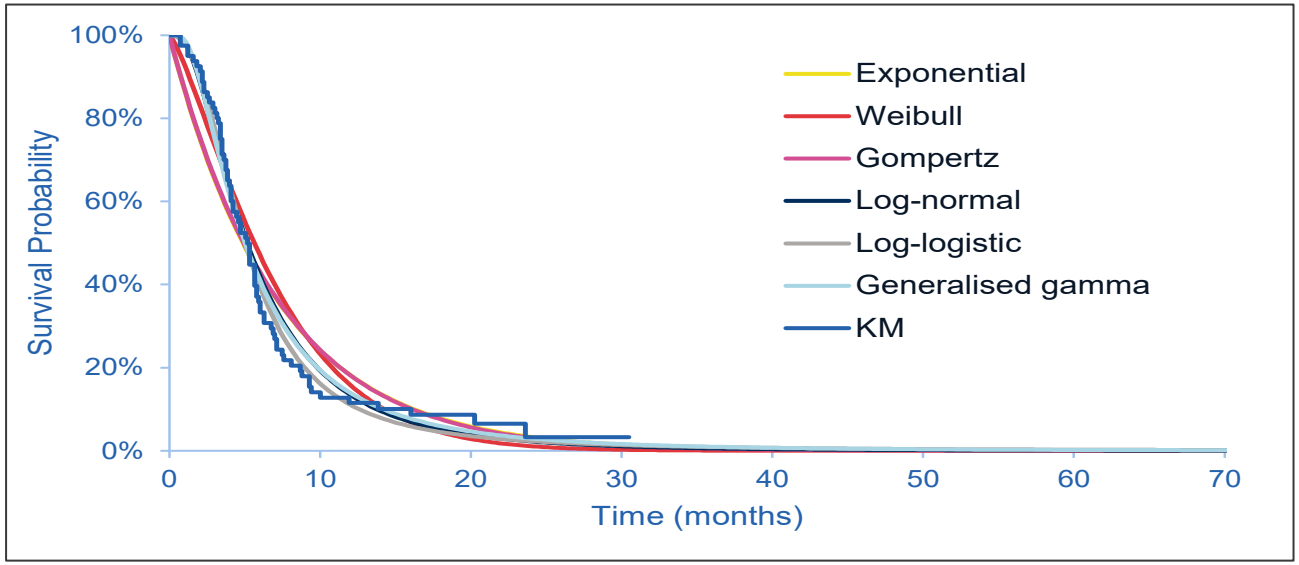
ABC-06 mFOLFOX+ASC



Company expert: 5-year survival >**0.1%**

Model	3-year OS	5-year OS
Exponential	1.6%	0.1%
Gen. gamma	1.5%	0.2%
Gompertz	0.2%	0.0%
Log-logistic	3.1%	1.2%
Log-normal	2.1%	0.4%
Weibull	0.3%	0.0%

ABC-06 ASC



Company expert: 5-year survival close to **0%**

Model	3-year OS	5-year OS
Exponential	0.6%	0.0%
Gen. gamma	1.0%	0.2%
Gompertz	0.5%	0.0%
Log-logistic	0.9%	0.3%
Log-normal	0.6%	0.1%
Weibull	0.0%	0.0%

ASC: Active symptom control; mFOLFOX: Modified oxaliplatin, L-folinic acid and fluorouracil; OS: Overall survival

ACD consultation comments (company)

5. A summary of relevant external data to estimate expected survival for the comparator groups (1)

Company comment

1. Updated ABC-06 publication provides additional detail on patient outcomes by tumour site:
   - ABC-06 may be over-estimating the outcomes for the indication in this appraisal because people with iCCA have a worse prognosis than eCCA
2. ClarIDHy, a phase 3 randomised trial, has been identified as a potential source of validation for survival estimates in a similar patient population:
   - When adjusted for crossover, the ClarIDHy placebo arm is consistent with outcomes from ABC-06 (see next slide)
3. Outcomes from other studies identified in MAIC support an OS extrapolation that predicts a minority of chemotherapy patients alive at 3 years, and almost no patients at 5 years.

ERG comment

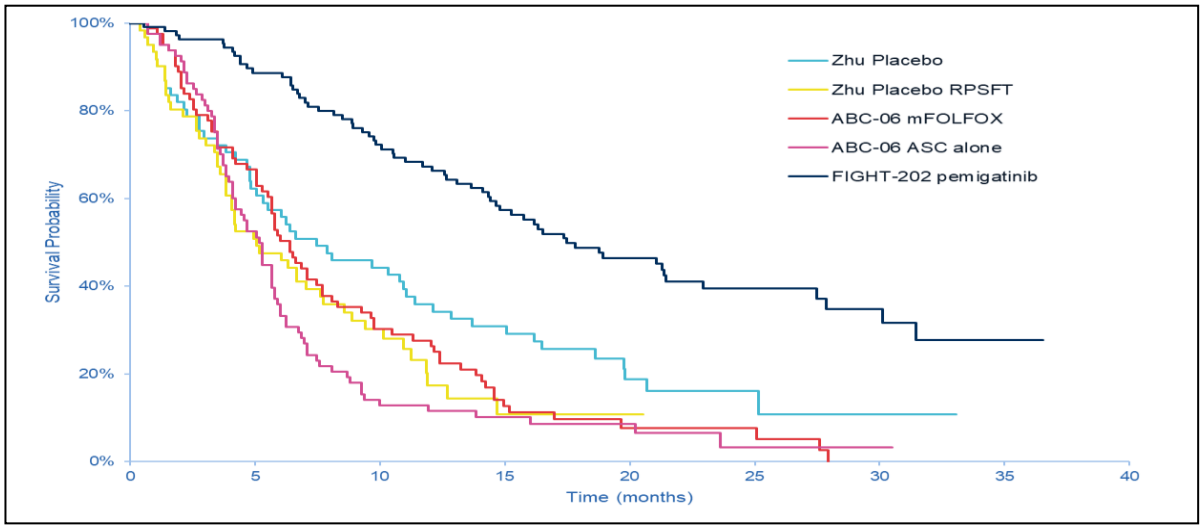
- Notes that people with iCCA had a worse prognosis at 6 months, but not at 12 months compared to eCCA
- Evidence does not reduce uncertainty for the population in this appraisal because it involves a comparison between different mutation subgroups and the unselected ABC-06 population.

ASC: Active symptom control; eCCA: extrahepatic cholangiocarcinoma; iCCA: intrahepatic cholangiocarcinoma; MAIC: Matching adjusted indirect comparison; OS: Overall survival

ACD consultation comments (company)

5. A summary of relevant external data to estimate expected survival for the comparator groups (2)

ClarIDHy (Zhu) OS vs. ABC-06 vs. FIGHT-202



ClarIDHy patient outcomes vs. ABC-06 vs. FIGHT-202

M	Zhu Placebo	Zhu Placebo RPSFT	ABC-06 mFOLFOX	ABC-06 ASC alone	FIGHT-202 pemi
6	57%	48%	52%	36%	89%
12	36%	17%	28%	12%	67%
18	26%	11%	10%	9%	49%
24	16%	N/A	8%	3%	39%
30	11%	N/A	N/A	3%	35%
36	N/A	N/A	N/A	N/A	28%

ERG comment

Population differences:

- The ClarIDHy trial was also for a molecular subpopulation i.e. iDH1 mutation
  - With 95% of patients with iCCA disease
- Similarity between the iDH1 and FGFR2 mutation populations in terms of proportion of patients with iCCA, does not necessarily equate to similar survival characteristics in patients with FGFR2 mutation.

FGFR: Fibroblast growth factor receptor; iCCA: intrahepatic cholangiocarcinoma M: Months; MAIC: Matching adjusted indirect comparison; OS: Overall survival;

Key modelling assumptions

Assumption	Company base case	ERG base case
Pemigatinib OS estimate:	Log-logistic	Log-logistic or gen. gamma
Pemigatinib PFS estimate	Log-normal	
Pemigatinib time on treatment (ToT)	Weibull	
ASC OS from ABC-06	Log-logistic	Log-logistic or gen. gamma
ASC PFS from ABC-06	Equal to PFS for mFOLFOX+ASC arm	
mFOLFOX+ACS OS from ABC-06	Log-logistic	Log-logistic or gen. gamma
mFOLFOX+ACS PFS from ABC-06	Log-normal	
Estimate of health state utility values	Regression model 3 excluding treatment status	
Independent/dependent models*	Dependent models	Independent models
Wastage costs	Included	
Genetic testing and OCT costs for pemigatinib	Included	

*Selected parametric curves were the same for pemigatinib when dependent models (HR) were used.
ASC: Active symptom control; mFOLFOX: Modified oxaliplatin, L-folinic acid and fluorouracil; OCT: Optical coherence tomography; OS: Overall survival; PFS: Progression-free survival; ToT: Time on treatment

Cost-effectiveness results: company base-case

Includes:
- Log-logistic OS extrapolation
- Log-normal PFS extrapolation
- Dependent models
- Genetic testing costs
- OCT costs

Fully incremental deterministic results (updated PAS price)

Technology	Total costs (£)	Total QALYs	Incr. costs (£)	Incr. QALYs	ICER (£/QALY)
ASC alone	[redacted]	[redacted]	-	-	-
mFOLFOX+ASC	[redacted]	[redacted]	[redacted]	[redacted]	154,593/Extendedly dominated*
Pemigatinib	[redacted]	[redacted]	[redacted]	[redacted]	45,029

Fully incremental probabilistic results (updated PAS price)

Technology	ICER (£/QALY)
mFOLFOX+ASC	Extendedly dominated*
Pemigatinib	43,736

Company's pairwise deterministic results versus mFOLFOX+ASC (updated PAS price)

Technology	Incr. costs (£)	Incr. QALYs	ICER (£/QALY)
mFOLFOX+ASC	-	-	-
Pemigatinib	[redacted]	[redacted]	42,076

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

ASC: Active symptom control; ICER: Incremental cost-effectiveness ratio; mFOLFOX: Modified oxaliplatin, L-folinic acid and fluorouracil; OCT: Optical coherence tomography; OS: Overall survival; PAS: Patient access scheme; QALY: Quality-adjusted life year

Scenario analysis – updated PAS price

Fully incremental deterministic results - independent parametric survival model scenarios

OS for all arms	OS extrapolation data	ICER (£/QALY) versus mFOLFOX+ASC	ICER (£/QALY) versus ASC	Pemi 3-year OS	Pemi 5-year OS
Log logistic*†	Unadjusted FIGHT-202	£45,123	£44,411	24.8%	12.5%
	FIGHT-202 adjusted using ASC ABC-06	£45,808	£45,010	25.2%	11.6%
	FIGHT-202 adjusted using ASC+mFOLFOX ABC-06	£45,051	£44,354	25.8%	11.9%
Generalised gamma†	Unadjusted FIGHT-202	£51,622	£52,866	24.2%	9.9%
	FIGHT-202 adjusted using ASC ABC-06	£52,116	£53,323	24.3%	8.4%
	FIGHT-202 adjusted using ASC+mFOLFOX ABC-06	£49,987	£51,307	25.5%	9.3%

* Company's preferred scenario (preferred dependent models in base case).

† ERG did not have a strong preference over any of the independent curves.

ASC: Active symptom control; ICER: Incremental cost-effectiveness ratio; mFOLFOX: Modified oxaliplatin, L-folinic acid and fluorouracil; OS: Overall survival; PAS: Patient access scheme; QALY: Quality-adjusted life year

Company expert: 5-year survival **10 to 13%**

Scenario analysis – updated PAS price

Fully incremental deterministic results - <u>dependent</u> parametric survival model scenarios

	ICER (£/QALY) versus mFOLFOX+ASC	ICER (£/QALY) versus ASC	Pemi 3-year OS	Pemi 5-year OS
Company base case (log-logistic)	£42,076	£45,029	24.8%	12.5%
Generalised gamma (OS extrapolation)	£49,629	£52,916	24.2%	9.9%
Exponential (OS and PFS extrapolation)	£46,935	£49,371	27.1%	11.4%

Company expert: 5-year survival **10 to 13%**

ASC: Active symptom control; ICER: Incremental cost-effectiveness ratio; mFOLFOX: Modified oxaliplatin, L-folinic acid and fluorouracil; OS: Overall survival; PFS: Progression-free survival; QALY: Quality-adjusted life year

Key issues

- Should dependent or independent models be used to extrapolate survival?
- Which is the most appropriate parametric curve?