Trifluridine–tipiracil for treating metastatic gastric or gastro-oesophageal junction cancer after 2 or more therapies [ID6167 review of TA669]

Slides for public observers

Technology appraisal committee C [4 October 2022]

Chair: Stephen O'Brien

Evidence assessment group: ScHARR

Technical team: Catie Parker and Ross Dent

Company: Servier

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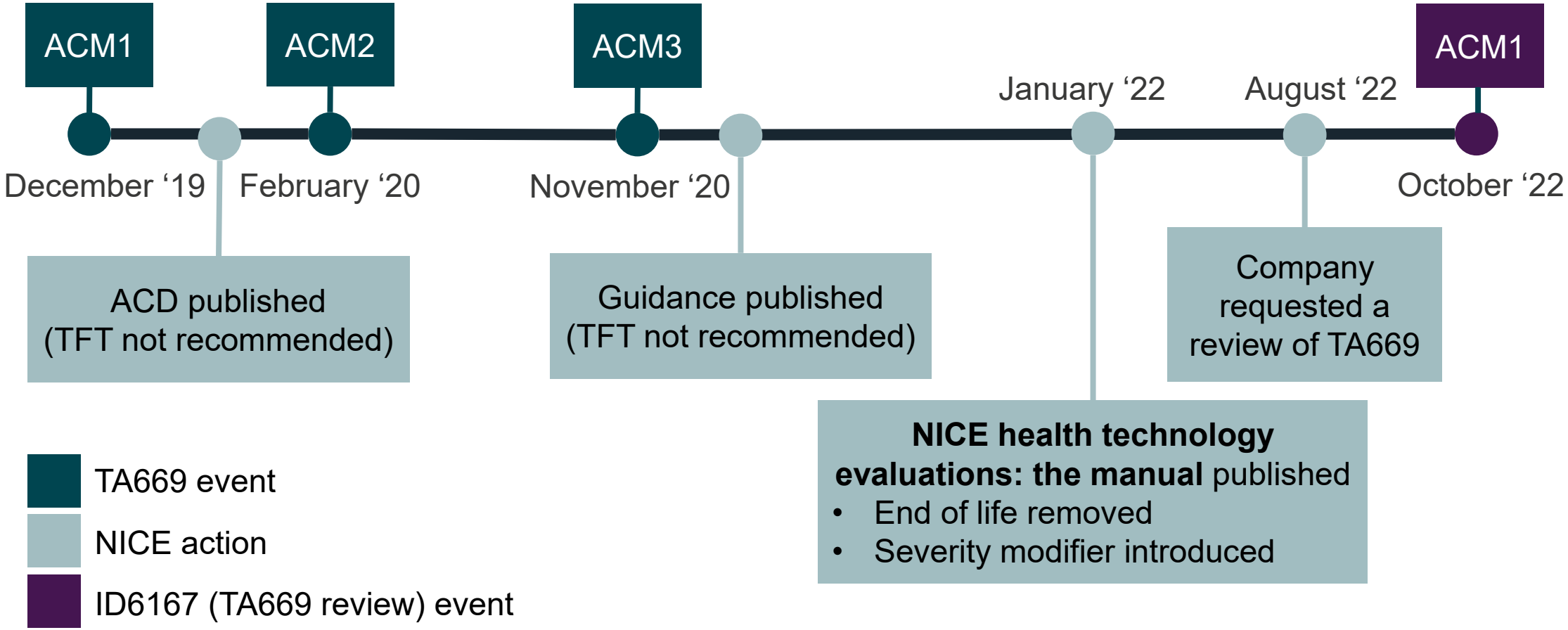
Timeline

Summary of key dates from TA669 and rapid review

Figure 1 Timeline of topic dates



Abbreviations: ACD, appraisal consultation document; ACM, appraisal committee meeting; TFT, trifluridine-tipiracil

TA669 Background

Trifluridine–tipiracil was not recommended

Disease background

- Gastric cancers are malignant growths of the stomach lining
- Symptoms can be vague and include unwanted weight loss, fluid in the abdomen and blood in stool
- Life expectancy after 2 previous treatments is between 2 and 4 months

Current care

- No standard 3rd line treatment options, best supportive care – no changes since TA669 published

Technology

- Trifluridine–tipiracil (Lonsurf, Servier) is indicated "for the treatment of adult patients with metastatic gastric cancer including adenocarcinoma of the gastroesophageal junction, who have been previously treated with at least two prior systemic treatment regimens for advanced disease"
- Recommended in TA405 for previously treated metastatic colorectal cancer
- Simple PAS discount – increase proposed for this appraisal

TA669 recommendation

- Trifluridine–tipiracil is **not recommended** for treating metastatic gastric cancer or gastro-oesophageal junction adenocarcinoma in adults who have had 2 or more systemic treatment regimens

Abbreviations: PAS, Patient Access Scheme

TA669 Committee discussion

Selected committee preferred assumptions and conclusions

Table 1 Committee assumptions and conclusions in the FAD

Issue	Committee preferred assumption or conclusion	FAD
Comparator	Best supportive care	3.2
Population	3rd line European subgroup from TAGS trial	3.3
Economic model	Suitable for decision making	3.5
Treatment duration function	Generalised gamma function	3.9
Survival function	Log-normal function	3.8
End of life criteria 1. Short life expectancy (≤24 months) 2. Life extension (≥3 months)	1. **Met**: Mean survival* of 6.5 months for best supportive care 2. **Not met**: Mean survival gain* of 2.7 months (41% increase compared with best supportive care) *Using committee's preferred assumptions	3.12
Cost-effectiveness estimates	Committee concluded that all ICERs, including the most plausible ICER based on its preferred assumptions, were substantially higher than £30,000 per QALY gained	3.13

Abbreviations: FAD, final appraisal document; ICER, incremental-cost effectiveness ratio; QALY, quality-adjusted life year

TA669 cost-effectiveness results

Committee's most plausible ICER was £49,771 per QALY

Table 2 Cost-effectiveness results from TA669

3L subgroup OS: log-normal new PAS	Arm	Total			Incremental			ICER (£/QALY)	OS gain (mean, months)
		Costs	QALY	LYs	Costs	QALY	LYs		
All regions	BSC	[redacted]	0.367	0.541					
	TFT	[redacted]	0.531	0.782	[redacted]	0.164	0.241	**£45,662**	**2.9 (+44%)**
Europe only*	BSC	[redacted]	0.371	0.547					
	TFT	[redacted]	0.527	0.774	[redacted]	0.156	0.227	**£49,771**	**2.7 (+41%)**

Table 3 Scenarios from TA669

3L Europe TTD scenarios	ICER
Exponential	£49,866
Weibull	£49,342
Gompertz	£49,197
Gen. gamma	£49,771
Log-normal	£52,902
Log-logistic	£53,557
OS scenario	ICER & LYG
Log-logistic	£45,168 +3.0 mos.

NICE tech team (at ACM3)

Main sources of uncertainty:

1. Potential unmeasured confounders in weighted analysis (effect not known)
2. Choice of parametric model for TTD (gen. gamma vs log-normal)

End of life criteria: mean OS gain is < 3 months but,

- Closer than analysis used for decision-making at ACM2: 1.7 mos. (+26%)
- Similar to proportional gain accepted in TA476: 2.4 months (+40%)

Abbreviations: ACM, appraisal committee meeting; BSC, best supportive care; ICER, incremental cost-effectiveness ratio; LY, life years; LYG, life years gained; OS, overall survival; PAS, patient access scheme; QALY, quality-adjusted life year; TFT, trifluridine–tipiracil; TTD, time to treatment discontinuation; 3L, 3rd line

Severity modifier

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Key issue: Severity modifier

Company and EAG agree that a 1.7 QALY weight is appropriate

Background: Company asked to submit evidence for severity modifier for committee's preferred analysis in TA669. No other changes.

Company

- Used ScHARR app for shortfall estimates
  - 3rd line TAGS European population: mean age of 62 and 33.3% female (committee's preference*)
  - 11.69 QALYs gained for population **without** disease
  - 0.37 QALYs gained for population **having BSC**
  - Proportional shortfall: 96.84%
  - Absolute shortfall: 11.3
- Higher QALY weight of 1.7 applies

*company base case is full 3rd line population from TAGS

EAG comments

- Support company's view that severity modifier of 1.7 appears appropriate

Table 3 NICE's QALY weights for absolute and proportional QALY shortfall

QALY weight	Proportional QALY shortfall	Absolute QALY shortfall
1	Less than 0.85	Less than 12
x1.2	0.85 to 0.95	12 to 18
x1.7	At least 0.95	At least 18

NICE's manual: QALY weightings for severity are applied based on absolute and proportional shortfall, whichever implies the greater severity level (6.2.18)

Is the QALY weight of 1.7 appropriate?

Abbreviations: BSC, best supportive care; EAG, external assessment group; QALY, quality-adjusted life year; ScHARR, School of Health and Related Research

Deterministic cost-effectiveness results

Table 4 Company and EAG results (deterministic)

No.	Scenario	Incremental costs versus BSC	Incremental QALYs versus BSC	ICER (£/QALY) versus BSC
1	Committee's preferred assumptions from TA669 **with severity modifier of 1**	[redacted]	[redacted]	£49,771
2	Committee's preferred assumptions from TA669 **with severity modifier of 1.7**	[redacted]	[redacted]	£29,347

Abbreviations: BSC, best supportive care; EAG, external assessment group; ICER, incremental-cost effectiveness ratio; QALY, quality-adjusted life year

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Thank you.