

Chair's presentation – PART 1

Midostaurin for untreated acute myeloid leukaemia

3rd appraisal committee meeting

Committee C

Lead team: Derek Ward, David Chandler, Steve O'Brien

ERG: CRD and CHE, University of York

NICE technical team: Kirsty Pitt and Sally Doss

Company: Novartis

21st March 2018

Recap of comments on ACD

Patient and professional organisations

- Joint response from professional groups accepts majority of committee's preferred adjustments to cost-effectiveness model
- Separation of survival curves in early stages of chemotherapy treatment suggests that main clinical benefit of midostaurin is from initial induction and consolidation therapy
- Patient organisation believes midostaurin does meet end of life criteria due to differences between trial population and UK population

Recap of comments on ACD

Company's response to ACD and new evidence

Response to ACD

- Comments on end of life considerations
- Comments on the mean age of population

New evidence

- Changes to the economic model
 - Survival after the cure point
 - Utility value in relapsed health state
 - Costs in the relapsed health state
 - Alternative age-adjusted utility values
- Proposed simple discount patient access scheme

Committee's discussion at second meeting (1)

Issue	Committee's discussion
Model structure	Committee's ACD conclusion: <ul style="list-style-type: none">• Surviving patients with relapsed disease should enter a cured health state after 3 years• Should be no health state costs after the cure point
Utility value in relapsed health state	Company argued 0.78 should be maximum utility value
Management costs in relapsed health state	Company revised costs from £4,884 to £2,000 per cycle
Age-adjusted utility values	Company presented a new method of adjustment for age

Committee's discussion at second meeting (2)

Issue	Committee's discussion
Survival after cure point	Company applied 2-fold increase in mortality rate after cure point
Cure point	Committee's ACD conclusion: <ul style="list-style-type: none"> • Uncertain – but moving the cure point earlier or later than company's base case (6.2 years) increases the ICER
Mean age of population in model	Company presented figure of ■ from Haemtaological Malignancy Research Network (HMRN)
End of life criteria	Committee's ACD conclusion: <ul style="list-style-type: none"> • Met: >3 months extension to life • Not met: life expectancy is over 24 months Company presented additional evidence from HMRN
Innovation	Committee's ACD conclusion: <ul style="list-style-type: none"> • Midostaurin is innovative, but benefits are captured in cost-effectiveness analysis

Update following second meeting

- Following release of the FAD to consultees and commentators, the company requested to submit an updated value proposition
- Therefore NICE suspended the FAD for consideration for appeal and the FAD was not published on the website

Company's revised analyses

Assumptions in company's new 'base' model	Explored analyses
<ul style="list-style-type: none"> Surviving patients with relapsed disease enter cured health state after 3 years Original calculation of time on treatment Company approach to utility value age adjustments Costs of adverse events associated with stem cell transplant included Trial-based model 	-
Management costs of £2,000/cycle for relapsed health state	-
Utility value of 0.655 in relapsed health state	Utility value of 0.78
Mean age of population 60 years	Mean age of ■ years
2-fold increased mortality rate after the cure point	4-fold increased rate
Cure point at 6.2 years	Cure point at 4 years Cure point at 7 years

Company's revised analyses results

List price analyses

Amendment	ICER midostaurin vs standard of care (£/QALY)	
	Individual change	
Company's new 'base' model*		■
1. Mean age of ■ years		■
2. Utility value in relapsed health state = 0.78		■
Further exploratory analyses		
3. 4-fold survival after the cure point		■
4a. Cure point at 4 years		■
4b. Cure point at 7 years		■

*analysis was seen at last committee meeting, calculated by the ERG

Company's revised analyses results

Including updated PAS

Amendment	ICER midostaurin vs standard of care (£/QALY)	
	Individual change	Cumulative change
Company's new 'base' model*	██████	-
1. Mean age of █████ years	██████	-
2. Utility value in relapsed health state = 0.78	██████	██████
Further exploratory analyses		
3. 4-fold survival after the cure point	██████	██████
4a. Cure point at 4 years	██████	-
1-3, 4a	-	██████
4b. Cure point at 7 years	██████	-
1-3, 4b	-	██████

The ERG has checked the revised economic model and is satisfied that the revised PAS and additional analyses have been correctly implemented by the company

*analysis was seen at last committee meeting, calculated by the ERG with the original PAS

Key issues

- Committee's ACD conclusion: end of life criteria not met
- What is the most plausible ICER for midostaurin compared with standard of care?