Nivolumab–relatlimab for untreated unresectable or metastatic melanoma

Slides for public
Confidential information redacted

Technology appraisal committee A, 7 November 2023

Chair: James Fotheringham

Lead team: Hugo Pedder, Alan Thomas, Patrick De Barr

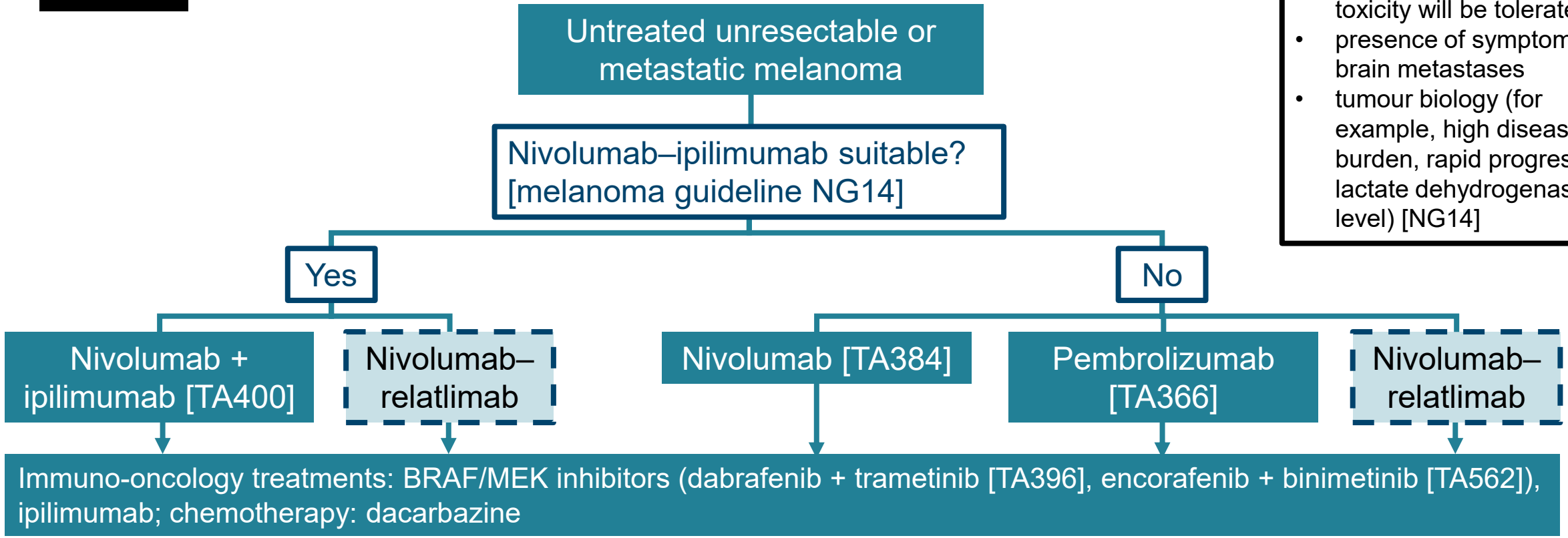
External assessment group: Liverpool Reviews and Implementation Group (LRiG)

Technical team: Emilene Coventry, Joanna Richardson, Janet Robertson

Company: Bristol-Myers Squibb

Treatment pathway

[redacted]



Factors to take into account when choosing treatment:

- comorbidities and performance status
- risk of treatment toxicity
- whether potential treatment toxicity will be tolerated
- presence of symptomatic brain metastases
- tumour biology (for example, high disease burden, rapid progression, lactate dehydrogenase level) [NG14]

Committee concluded:

- nivolumab–relatlimab would mainly be an alternative to monotherapy in NHS
- could also be an alternative if nivolumab plus ipilimumab an option because MA for all patients

NICE

Abbreviations: MA: marketing authorisation; NG, NICE guideline; TA, technology appraisal

Committee's preferred assumptions after ACM1

Generalisability – committee concluded that available trial evidence could be generalised to:

- everyone in the NHS who could be offered nivolumab–relatlimab
- 12 to 18 year olds

Model input	Committee's preferred assumption (ACM1)	Company/EAG base case (ACM1)
Nivo–rela PFS/OS	Investigator assessed from RELATIVITY-047	Both
Nivo PFS/OS	Investigator assessed from RELATIVITY-047	Both
Nivo + ipi PFS/OS	Constant HRs from company's adjusted ITC	Both
Pembrolizumab PFS/OS	Set equal to nivolumab	EAG
Stopping rule for combination immunotherapies	2 years	Company
Subsequent treatment costs	When **comparing** nivolumab–relatlimab **to the monotherapies**: • **company's proportions** of subsequent treatments **preferred** for nivolumab–relatlimab arm When **comparing** nivolumab–relatlimab **to nivolumab plus ipilimumab:** • **EAG's proportions** of subsequent treatments **preferred** for the nivolumab–relatlimab arm	Dependent on comparison

NICE Because of remaining OS uncertainty, committee agreed acceptable ICER would be below the range usually considered cost effective (~£25,000 per QALY)

Subsequent treatments

Subsequent treatments pre ACM1 modelled for intervention and comparator by company and EAG (differed for nivolumab-relatlimab arm only)

Subsequent treatments	Nivo–rela (%)	Nivolumab (%)	Pembrolizumab (%)	Nivo + ipi (%)
Dabrafenib + trametinib	19.26	19.26	19.26	19.26
Encorafenib + binimetinib	19.26	19.26	19.26	19.26
Ipilimumab	24.59 [company]; 61.48 [EAG]	61.48	61.48	0
Best supportive care or clinical trials (costed as chemotherapy)	36.89 [company]; 0 [EAG]	0	0	61.48

Requested analyses post ACM1 - comparing nivolumab-relatlimab to monotherapies

- use same company values in both the nivolumab and pembrolizumab arms as nivolumab-relatlimab arm
- plus analyses using proportions suggested by clinical experts in both the nivo-rela and monotherapy arms

Subsequent treatments	Nivo-rela (%)	Nivolumab (%)	Pembrolizumab (%)
Dabrafenib + trametinib	19.26	19.26	19.26
Encorafenib + binimetinib	19.26	19.26	19.26
Ipilimumab	24.59; 20	24.59; 20	24.59; 20
Best supportive care or clinical trials (costed as chemotherapy)	36.89; 41.48	36.89; 41.48	36.89; 41.48

Cost effectiveness results compared with monotherapies

Nivolumab–relatlimab compared with nivolumab

Model assumptions for subsequent treatments	Incremental costs (£)	Incremental QALYs	ICER (£)
Company values (deterministic)	[redacted]	[redacted]	[redacted]
Company values (probabilistic)	[redacted]	[redacted]	[redacted]
Clinical expert's values (deterministic)	[redacted]	[redacted]	[redacted]
Clinical expert's values (probabilistic)	[redacted]	[redacted]	[redacted]

Nivolumab–relatlimab compared with pembrolizumab

Model assumptions for subsequent treatments	Incremental costs (£)	Incremental QALYs	ICER (£)
Company values (deterministic)	[redacted]	[redacted]	[redacted]
Company values (probabilistic)	[redacted]	[redacted]	[redacted]
Clinical expert's values (deterministic)	[redacted]	[redacted]	[redacted]
Clinical expert's values (probabilistic)	[redacted]	[redacted]	[redacted]

Abbreviations: ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year

Cost effectiveness results compared with nivolumab + ipilimumab

Nivolumab–relatlimab compared with nivolumab plus ipilimumab (deterministic)

Model assumptions	Inc costs (£)	Inc QALYs	ICER (£)
EAG subsequent treatment costs (shown in previous part 2 slides [slide 4, R7])	[redacted]	[redacted]	[redacted]

Subsequent treatments	Nivolumab-relatlimab	Nivolumab-ipilimumab
Dabrafenib + trametinib	19.26	19.26
Encorafenib + binimetinib	19.26	19.26
Ipilimumab	61.48 [EAG]	0
Best supportive care or clinical trials (costed as chemotherapy)	0 [EAG]	61.48

Using any other values of subsequent treatments in the nivolumab–relatlimab arm would lower the ICER

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

OS gains uncertain

Treatment	Before progression	After progression	All patients
Nivolumab–relatlimab	[redacted]	[redacted]	[redacted]
Nivolumab	[redacted]	[redacted]	[redacted]
Nivolumab + ipilimumab	[redacted]	[redacted]	[redacted]
Pembrolizumab	[redacted]	[redacted]	[redacted]

- Background mortality on first-line nivolumab–relatlimab twice that of comparators after progression
- Clinical experts:
  - plausible for some people to reach background mortality after progression
  - immunotherapies could affect OS differently to PFS; those on 2nd-line immunotherapy likely to have better long-term survival
- Post ACM1 information
  - No new OS data available from RELATIVITY-047
  - Fewer people in trial (which was a global trial) on first-line nivolumab–relatlimab had second-line ipilimumab than those on first-line nivolumab

Subsequent treatments from RELATIVITY-047

Subsequent systemic therapy	Nivolumab–relatlimab (n=355) n (%)	Nivolumab (n=359) n (%)
Any	[redacted]	[redacted]
PD-L1 and/or CTLA-4 inhibitors	[redacted]	[redacted]
Nivolumab + ipilimumab	[redacted]	[redacted]
Nivolumab monotherapy	[redacted]	[redacted]
Ipilimumab monotherapy	[redacted]	[redacted]
Pembrolizumab monotherapy	[redacted]	[redacted]
Avelumab monotherapy	[redacted]	[redacted]
BRAF and/or MEK inhibitors	[redacted]	[redacted]
Trametinib + Dabrafenib	[redacted]	[redacted]
Encorafenib + Binimetinib	[redacted]	[redacted]
Dabrafenib	[redacted]	[redacted]
Vemurafenib	[redacted]	[redacted]