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Intracranial activity of encorafenib and binimetinib followed by radiotherapy in patients with BRAF mutated melanoma and brain metastasis: Preliminary results of the GEM1802/EBRAIN-MEL phase II clinical trial

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Background

Systemic treatment for patients (pts) with *BRAF*- mutated (mut) melanoma (mel) and brain metastasis (BMs) include immunotherapy and targeted therapy. COMBI-MB clinical trial analyzed the role of dabrafenib + trametinib, with an intracranial response rate (icRR) of 58% for asymptomatic and 59% for symptomatic pts. Encorafenib + binimetinib (EB) has not been prospectively evaluated in this scenario.

Methods

GEM1802 (NCT03898908) is a prospective phase II clinical trial that evaluates EB (450 mg pd E + 45 mg bd B) in pts with BMs during 56 days (d) followed by brain radiotherapy (RDT) and EB until disease progression. Two cohorts (C) were planned: C1 (N=48), asymptomatic pts; and C2, symptomatic pts (N=15). Primary endpoint is icRR after 56d of EB (before RDT) in C1. Secondary endpoints are extracranial RR, intracranial progression free survival (icPFS), PFS, overall survival and safety. In addition, this study will explore if RDT could improve the duration of response with EB.

Results

We report preliminary results of icRR for first 25 pts with response evaluation after 56d of EB. 14 pts from C1 and 11 from C2 were evaluable for this analysis. icRR was 64.3% and 63.6% in C1 and C2 respectively. Partial response (PR), complete response (CR), stable disease (SD) and progressive disease (PD) as well as G3-4 AEs are described in the table. 71.4% pts in C1 and 72.7% in C2 received RDT following first 56 days of EB. Table: 1038MO

	C1 (asymptomatic)	C2 (symptomatic)		
N	14	11		
Previous systemic treatment (%)	21.4	18.2		
Brain Target Tumor Burden (mean, mm)	34.5	54.3		
		1	50	27.3
		2-3	42.8	45.5
		>3	7.1	27.3
		Extracranial disease	85.7	100
		icRR (95% CI)	64.3 (35-87)	63.6 (31-89)
		PR	57.1	54.5
		CR	7.1	9.1
%		SD	35.7	36.4
		PD	0	0

	C1 (asymptomatic)	C2 (symptomatic)
6 month icPFS	70.1	64.3
Whole brain RDT	28.6	45.5
Radiosurgery/SBRT	50	33.3
Related G3-4 AEs	23.5	13.3

Conclusions

These results are in line with previous data reported for other targeted therapies in this setting, demonstrating a high response rate that is independent of symptomatic status of the pts. Based on this analysis, planned enrollment will continue until completion of accrual.

Clinical trial identification

NCT03898908.

Legal entity responsible for the study

Spanish Melanoma Group (GEM).

Funding

Pierre Fabre.

Disclosure

I. Marquez-Rodas: Financial Interests, Personal, Advisory Board: BMS; Financial Interests, Personal, Advisory Board: MSD; Financial Interests, Personal, Advisory Board: Novartis; Financial Interests, Personal, Advisory Board: Pierre Fabre; Financial Interests, Personal, Advisory Board: Roche; Financial Interests, Personal, Advisory Board: GSK; Financial Interests, Personal, Advisory Board: AstraZeneca; Financial Interests, Personal, Advisory Board: Celgene; Financial Interests, Personal, Advisory Board: Regeneron; Financial Interests, Personal, Advisory Board: Sanofi; Financial Interests, Personal, Advisory Board: Merck Serono; Financial Interests, Personal, Advisory Board: Highligh Therapeutics; Financial Interests, Personal, Advisory Board: Bioline Rx; Financial Interests, Personal and Institutional, Invited Speaker, GEM1802 clinical trial: Pierre Fabre; Financial Interests, Institutional, Invited Speaker, GEM1801 clinical study: Novartis; Financial Interests, Institutional, Invited Speaker, GEM1801 clinical study: BMS; Financial Interests, Institutional, Invited Speaker, GEM1801 clinical study: Roche; Financial Interests, Institutional, Invited Speaker, GEM1801 clinical study: Pierre Fabre; Financial Interests, Institutional, Invited Speaker, GEM1801 clinical study: Incyte; Financial Interests, Institutional, Invited Speaker, GEM1801 clinical study: MSD; Financial Interests, Institutional, Invited Speaker, National coordinator of Spotlight 203 clinical trial: Highlight Therapeutics; Non-Financial Interests, Invited Speaker: Spanish Melanoma Group. A. Arance: Financial Interests, Personal, Invited Speaker: Pierre Fabre; Financial Interests, Personal, Advisory Role: Pierre Fabre; Financial Interests, Personal, Other, travel and accommodation: Pierre Fabre; Financial Interests, Personal, Research Grant: Pierre Fabre; Financial Interests, Personal, Invited Speaker: Novartis; Financial Interests, Personal, Advisory Role: Novartis; Financial Interests, Personal, Other, travel and accommodation: Novartis; Financial Interests, Personal, Research Grant: Novartis; Financial Interests, Personal, Invited Speaker: Roche; Financial Interests, Personal, Advisory Role: Roche; Financial Interests, Personal, Other, travel and accommodation: Roche; Financial Interests, Personal, Research Grant: Roche; Financial Interests, Personal, Invited Speaker: BMS; Financial Interests, Personal, Advisory Role: BMS; Financial Interests, Personal, Other, travel and accommodation: BMS; Financial Interests, Personal, Research Grant: BMS; Financial Interests, Personal, Invited Speaker: MSD; Financial Interests, Personal, Advisory Role: MSD; Financial Interests, Personal, Invited Speaker, travel and accommodation: MSD; Financial Interests, Personal, Research Grant: MSD; Financial Interests, Personal, Invited Speaker: MERCK; Financial Interests, Personal, Advisory Role: MERCK; Financial Interests, Personal, Other, travel and accommodation: MERCK; Financial Interests, Personal, Research Grant: MERCK; Financial Interests, Personal, Invited Speaker: Sanofi; Financial Interests, Personal, Advisory Role: Sanofi; Financial Interests, Personal, Other, travel and accommodation: Sanofi; Financial Interests, Personal, Research Grant: Sanofi; Financial Interests, Personal, Research Grant: Amgen. M.A. Berciano Guerrero: Financial Interests, Personal, Invited Speaker: BMS; Financial Interests, Personal, Invited Speaker: MSD; Financial Interests, Personal, Invited Speaker: Pierre Fabre; Financial Interests, Personal, Invited Speaker: Roche; Financial Interests, Personal, Invited Speaker: Pfizer; Financial Interests, Personal, Invited Speaker: Sanofi; Financial Interests, Personal, Invited Speaker: Eisai; Financial Interests, Personal, Invited Speaker: Pharmamar; Financial Interests, Personal, Invited Speaker: Kyowa Kirin; Financial Interests, Personal, Advisory Role: BMS; Financial Interests, Personal, Advisory Role: MSD; Financial Interests, Personal, Advisory Role: Pierre Fabre; Financial Interests, Personal, Advisory Role: Roche; Financial Interests, Personal, Advisory Role: Pfizer; Financial Interests, Personal, Advisory Role: Sanofi; Financial Interests, Personal, Advisory Role: Eisai; Financial Interests, Personal, Advisory Role: Pharmamar. M. Gonzalez Cao: Financial Interests, Personal, Invited Speaker: Roche; Financial Interests, Personal, Invited Speaker: MSD; Financial Interests, Personal, Invited Speaker: BMS; Financial Interests, Personal, Invited Speaker: Novartis; Financial Interests, Personal, Invited Speaker: Pierre Fabre; Financial Interests, Personal, Invited Speaker: AstraZeneca; Financial Interests, Personal, Research Grant: Roche; Financial Interests, Institutional, Funding: BMS; Financial Interests, Institutional, Funding: Roche; Financial Interests, Institutional, Funding: AstraZeneca; Financial Interests, Institutional, Funding: Apexigen; Financial Interests, Personal, Advisory Role: Pierre

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