2021 ESMO congress

INTRACRANIAL ACTIVITY OF ENCORAFENIB AND BINIMETINIB FOLLOWED BY RADIOTHERAPY IN PATIENTS WITH *BRAF* MUTATED MELANOMA AND BRAIN METASTASIS: PRELIMINARY RESULTS OF THE GEM1802 PHASE II CLINICAL TRIAL

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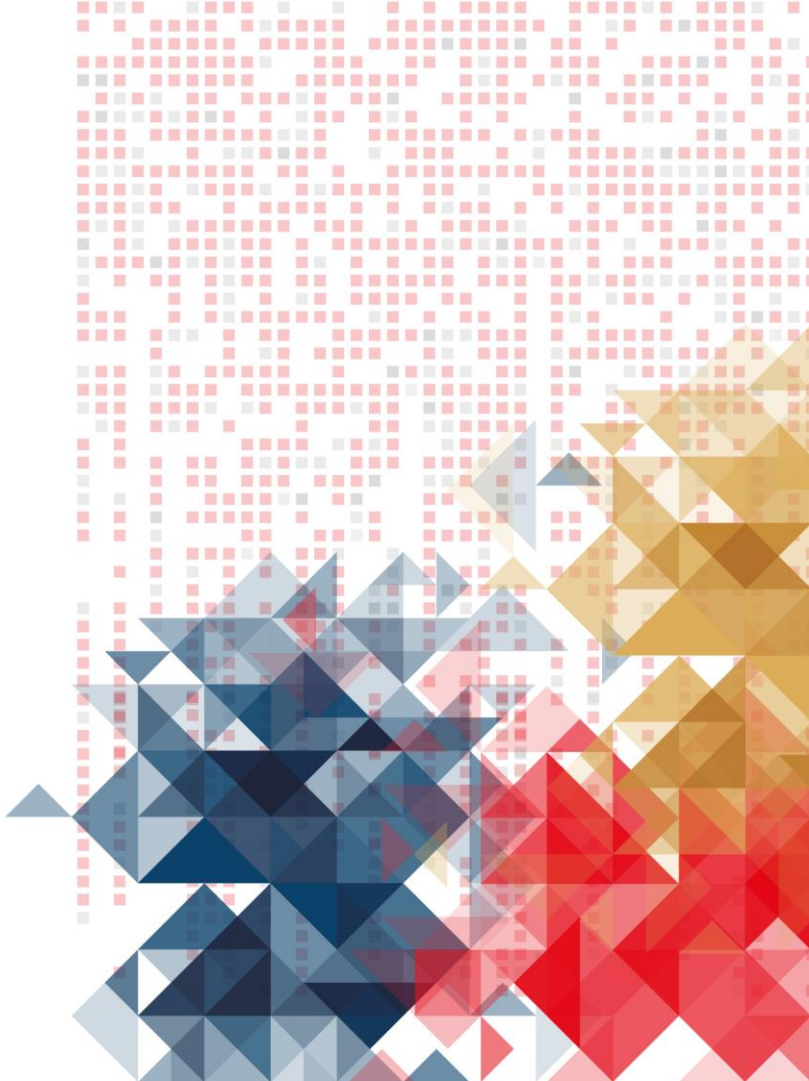
GEM
Grupo Español Multidisciplinar de Melanoma



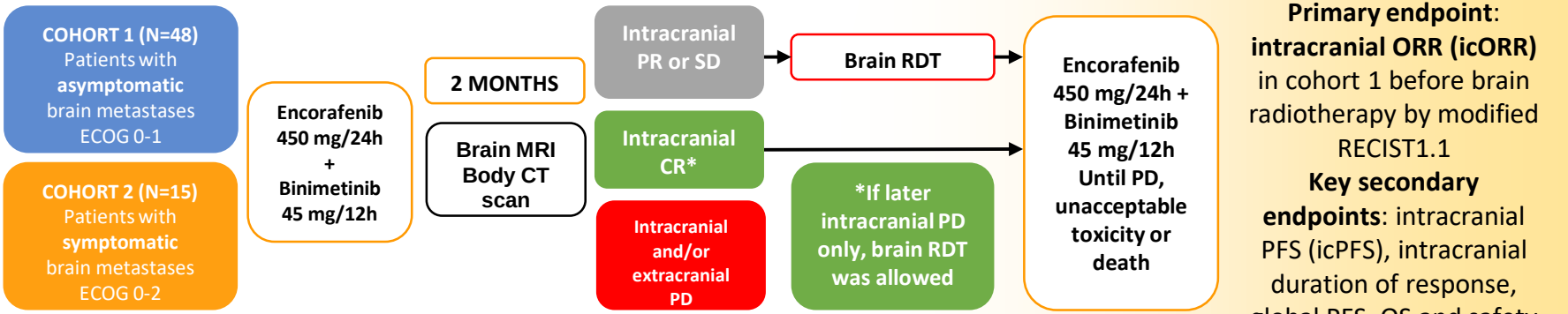
DECLARATION OF INTERESTS

- **Dr. Iván Márquez-Rodas financial interests**
  - Advisory Board: BMS, MSD, Novartis, Pierre Fabre, Roche, GSK, Astrazeneca, Celgene, Regeneron, Sanofi, Merck Serono, Highlight Therapeutics, Bioline Rx.

- **Funding current study**
  - Grupo Español Multidisciplinar de Melanoma (GEM) through Pierre Fabre grant.

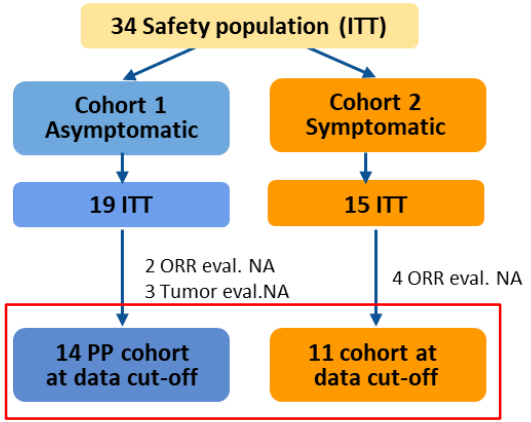
RATIONALE, OBJECTIVES & STUDY DESIGN

- Patients with *BRAF* mutated melanoma and brain metastases can benefit from both immunotherapy (IT) and targeted therapy (TT) [1,2,3].
- Duration of response (DOR) seems to be shorter with TT than observed with IT, whereas IT seems to be less active in symptomatic patients that need corticosteroids.
- COLUMBUS ph3 clinical trial demonstrated superiority of encorafenib + binimetinib (EB) over BRAF inhibition monotherapy, but excluded patients with brain metastases [4]
- **GEM1802/EBRAIN-MEL** (NCT03898908) is a ph2 single arm clinical trial that:
  - Evaluates the activity of EB in patients with asymptomatic and symptomatic *BRAF* mutated melanoma and brain metastases (at least one with 5-50 mm size)
  - Explores if the addition of radiotherapy after 2 months of EB could improve DOR



(1) Long ASCO 2021; (2) Tawbi Neuro Oncol 2021; (3) Davies Lancet Oncol 2017; (4) Dummer ASCO 2021.

RESULTS: PATIENTS´ CHARACTERISTICS

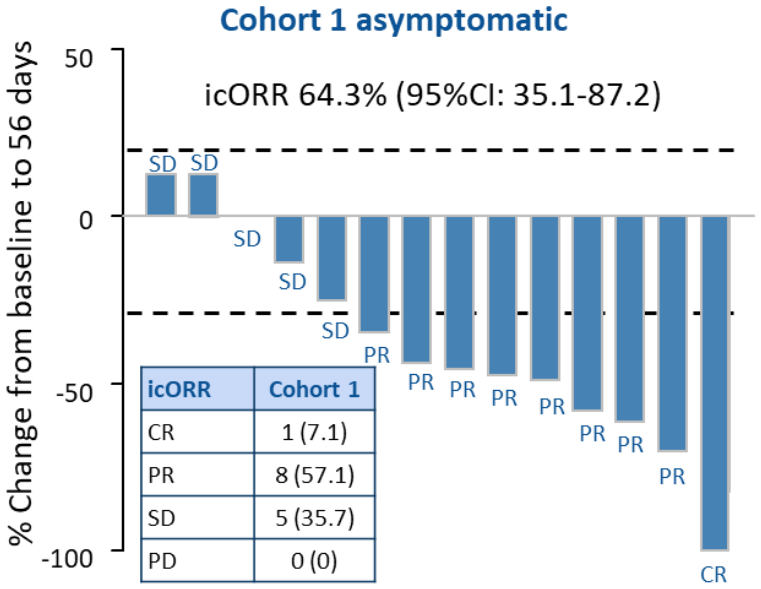


Characteristic	Cohort 1 (Asymptomatic) n = 14	Cohort 2 (Symptomatic) n = 11
Age (range), years	52.2 (18-85)	44 (21-79)
Gender, n (%)		
Male	7 (50)	6 (54.5)
Female	7 (50)	5 (45.5)
ECOG performance status, n (%)		
0	11 (78.6)	2 (18.2)
1	3 (21.4)	7 (63.6)
2	0 (0)	2 (18.2)

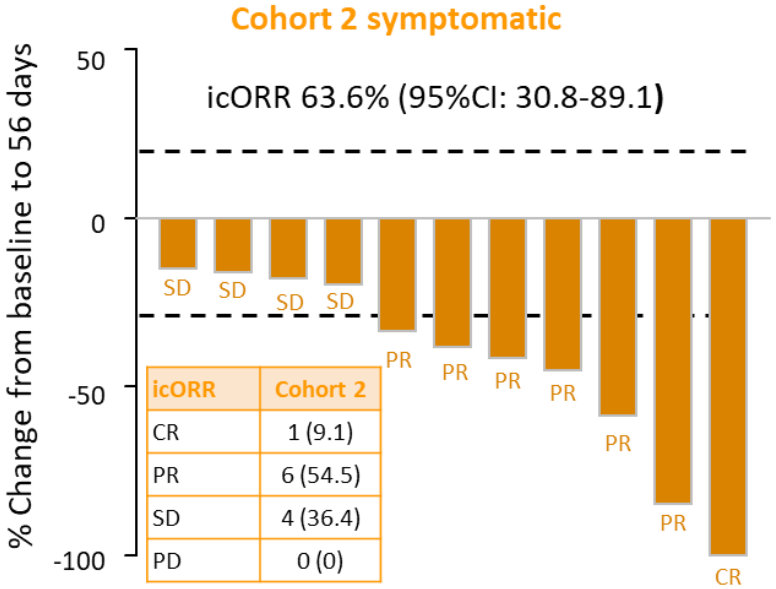
Characteristic	Cohort 1 (Asymptomatic) n = 14	Cohort 2 (Symptomatic) n = 11
BRAF genotype, n (%)		
V600E	12 (85.7)	10 (90.9)
V600K	2 (14.3)	1 (9.1)
Number of brain lesions, n (%)		
1	7 (50)	3 (27.3)
2-3	6 (42.8)	5 (45.5)
>3	1 (7.1)	3 (27.3)
Brain Target Tumor Burden (range), mm		
Median sum of diameters	27 (10-112)	46 (20-134)
Extracraneal metastasis, n (%)		
Yes	12 (85.7)	11 (100)
No	2 (14.3)	0 (0)
Lactate dehydrogenase level, n (%)		
Normal (≤ULN)	8 (57.1)	7 (63.6)
Elevated (>ULN)	5 (35.7)	4 (36.4)
Receiving steroid therapy, n (%)		
Yes	7 (50)	11 (100)
No	7 (50)	0 (0)
Previous systemic anticancer treatment, n (%)		
Yes	3 (21.4)	2 (18.2)
No	11 (78.6)	9 (81.8)

ITT: intention to treat; NA: non available; PP: per protocol

RESULTS: icORR and RDT received



icORR	Cohort 1
CR	1 (7.1)
PR	8 (57.1)
SD	5 (35.7)
PD	0 (0)

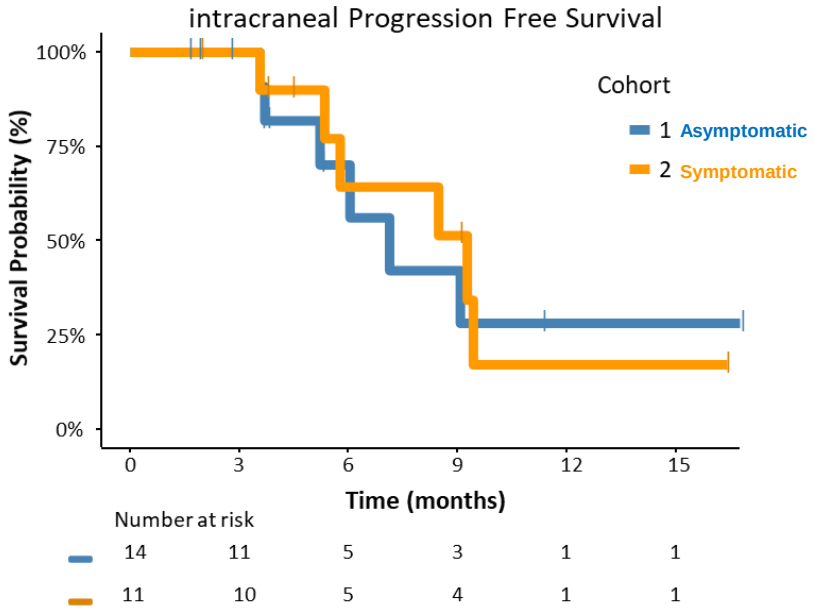


icORR	Cohort 2
CR	1 (9.1)
PR	6 (54.5)
SD	4 (36.4)
PD	0 (0)

Radiotherapy after 2 mo EB	Cohort 1	Cohort 2
RT any, n (%)	10 (71.4)	8 (72.7)
Whole Brain RT, n (%)	4 (40)	5 (63)
Radiosurgery/SRS, n (%)	6 (60)	3 (37)

RESULTS: icPFS and toxicity

icPFS	6m rate, % (95% CI)	Median (95% CI), m
Cohort 1	70.1 (46.5-100)	7.1 (5.2-NA)
Cohort 2	64.3 (38.5-100)	9.3 (5.8-NA)



TOXICITY

Safety population	Cohort 1 (Asymptomatic)	Cohort 2 (Symptomatic)
	n = 17	n = 15
Toxicities EB related, n (%)	14 (82.4)	9 (60)
Toxicities RT related, n (%)	0 (0)	1 (6.7)
G3-4 Toxicities EB related, n (%)	4 (23.5)	2 (13.3)
G3-4 Toxicities RT related, n (%)	0 (0)	1 (6.7)*
SAE related	1 (5.9)#	1 (6.7)*

*vomiting and #pancreatitis that required hospitalization
There were no deaths associated to EB treatment or RT.

CONCLUSIONS

- In this preliminary analysis, encorafenib and binimetinib showed intracranial activity in patients with *BRAF* mutated melanoma and brain metastases.
- These results are in line with previously described with other targeted therapies (i.e dabrafenib and trametinib) and seem to be independent of the presence of symptoms.
- The safety profile of adding radiotherapy could make this approach feasible, although longer follow up is needed in order to better characterize this strategy.

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