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G - MELANOMA AND SKIN CANCERS

G4 Metastatic melanoma patients treated with Braf and Mek inhibitors: Patterns of progression. An Italian Melanoma Intergroup study

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Background: Progression patterns data after BRAF +MEK inhibitors (I) could help clinicians in choosing the treatment strategy among the multiple available options in the BRAF v600 melanoma setting. We analysed outcomes in pts treated with BRAF+MEK i to characterize pts with rapid progression.

Methods: In this multicenter retrospective analisis, data were collected from 164 consecutive pts affected by BRAF v600 metastatic melanoma and treated with BRAF+MEK i from February 2012 to April 2017.

Results: 64 patients were enrolled. Baseline LDH was elevated in 68(41%)pts, baseline number of metastatic organs were 1, 2, 3 and more in 52(32%), 52(32%), 29(18%) and 32(19%) pts. BRAF+MEK i administered were dabrafenib+trametinib in 151 pts and vemurafenib+cobimetinib in 13 pts, and they were adiministered in first line in 129(79%)pts. Best response was CR, PR, SD and PD in 27, 87, 17 and 2 pts. On cutoff

date, progression was observed in 104(63%) pts - 60(37%) pts still on treatment. mPFS was 9,83(1-54,7+) months: significant difference in PFS was showed in pts with normal baseline LDH or high LDH (13.2 vs 6.3 months, $p < 0.0001$), and in pts with number of metastatic organs lower or higher then 2 (13,4 vs 7 months, $p < 0.0001$). mOS was 18.3(1-62,5+) months: significant difference in OS was showed in pts with normal baseline LDH or high LDH had (24,7 vs 10 months, $p < 0.0006$), and in pts with number of metastatic organs lower or higher then 2 (25.9 vs 10 months, $p < 0.0003$). Among 104 progressed pts, 72 (69%) pts died, mOS after progression was 2,5 months (0,5-42+ months); Subsequent treatments were administered in 44(42%) pts. Duration of response (DR) was defined as time from BRAF+MEK i best response to progression of disease. Significant difference in OS after BRAF+MEK i progression was observed in pts with DR < 6 months(77 pts) or > 6 months (27 pts) (2 vs 8,3 months, $p < 0.0023$) and in pts with number of metastatic organs after progression lower or higher then 3 (4,5 vs 2 months, $p < 0.022$).

Conclusion: DR and extension of progression during BRAF+MEK I are factors that can be useful to identify pts with lower OS after progression, in addiction to known parameters like LDH and baseline number of metastatic organs.