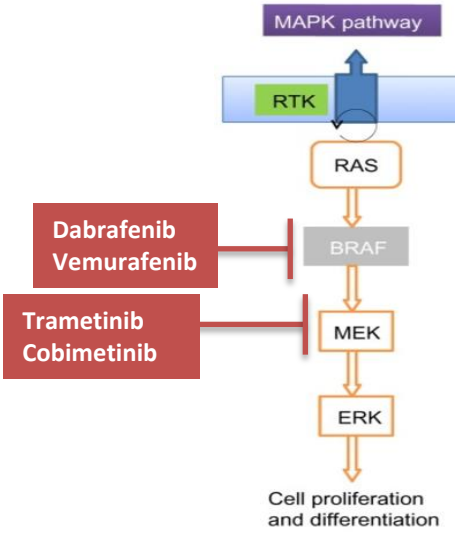
EXPERIENCE WITH BRAF AND MEK INHIBITORS IN THE TREATMENT OF METASTASIC MELANOMA IN A THIRD LEVEL UNIVERSITY HOSPITAL

A. Comes[1], G. Castells[2], E. Carcelero[2], G. Riu[2].
[1]Hospital Sant Joan de Déu, Pharmacy, Barcelona, Spain. [2]Hospital Clínic, Pharmacy, Barcelona, Spain.

BACKGROUND

The MAPK-pathway is a signal transduction cascade involved in the uncontrolled proliferation of many cancers. Mutations that active those pathways occur in more than 90% of melanomas. This has led to the development of dabrafenib and vemurafenib (target V600E/K BRAF), and trametinib and cobimetinib (target MEK1/2).



PURPOSE

To describe our experience in terms of effectivity and safety on the use of BRAF/MEK inhibitors in metastatic melanoma (MM) with activated MAPK-pathway.

MATERIAL AND METHODS

Retrospective observational study including patients with MM who received treatment with dabrafenib, trametinib, vemurafenib and/or cobimetinib.

Clinical data were collected from electronic patients' medical records, from the treatment prescription until May 2017, including: age, gender, ECOG, prior immunotherapy and chemotherapy lines, toxicity and the treatment discontinuation reason.

Response was measured as the time period from the start of treatment to the date of documentation of progression or lost to follow up (PFS).

RESULTS

62 BRAF mutated patients (48.39% male) with a median age of 55 years (18-89), and a medium ECOG of 1 (47%). 16.13% received prior immunotherapy.

- **80%** SKIN DISORDER
- **64%** ELEVATED LIVER ENZYME
- **59%** ASTHENIA MYALGIA
- **55%** GASTROINTESTINAL DISORDERS
- **36%** FEVER
- **23%** ANEMIA NEUTROPENIA
- **22%** OCULAR DISORDERS

All AE were classified as grade 1 or 2 *(according to the CTCAE)* and responded to supportive treatment.

✓47% of patients were treated with dabrafenib+trametinib, 16% with vemurafenib+cobimetinib, 13% with dabrafenib, 11% with vemurafenib, and 13% were combinations.
✓68% of BRAF/MEK inhibitors were prescribed as a first line treatment, 26% as second line and 3% as a third or more lines.
✓52% of treatment discontinuations were due to disease progression, 22.58% toxicity and 8.06% death.
✓Data of median PFS are available for 54 patients: 5.8 months for dabrafenib, 5.4 months for dabrafenib+trametinib, 1.34 months for vemurafenib and 7.48 months for vemurafenib+cobimetinib. These results are inferior compared with the pivotal studies.

CONCLUSION

The majority of BRAF mutated patients in our hospital with MM began with BRAF/MEK inhibitors as first line treatment. AE were frequent, but manageable. PFS was lower than pivotal studies. However we need information in more patients to confirm these results.