EFFECTIVENESS AND SAFETY OF BRAF/MEK INHIBITORS IN ADVANCED OR METASTATIC MELANOMA IN TWO TERTIARY HOSPITALS

BACKGROUND AND IMPORTANCE
Dabrafenib/trametinib and vemurafenib/cobimetinib: increased significantly Progression-Free Survival (PFS) and Overall Survival (OS) in patients with advanced or metastatic melanoma with BRAF mutations, in phase 3 Clinical Trials.

OBJECTIVE
To assess the effectiveness and safety of vemurafenib/cobimetinib and dabrafenib/trametinib, in patients with locally advanced or metastatic melanoma in real life.

MATERIAL AND METHODS:
• Design: retrospective, multicenter, observational study.
• Treatment: vemurafenib/cobimetinib or dabrafenib/trametinib in patients with BRAF-mutated melanoma.
• Variables collected: sex, age, stage, Performance Status (PS), previous treatments, duration of treatment and response, dose received and dose adjustments.
• Variables evaluated: PFS, OS, adverse events (AE), withdrawal rate and reason for it.

RESULTS:
42 patients analyzed
15 Women
Median 62.4 years old
81% metastatic melanoma
1st line: 71.4% vemurafenib/cobimetinib
14.3% dabrafenib/trametinib
Vemurafenib/cobimetinib (n=20), dabrafenib/trametinib (n=13), dabrafenib (n=1), both drugs (n=8) --> 38 patients analyzed, 4 loss of follow-up.

Effectiveness and safety:
- **Vemurafenib/trametinib**: median PFS 9.71 (IC95%:5.77-NA); median OS 18.5 (IC95%:11.9-NA). Median duration of treatment: 99 (IR:20-243).
  - 100% AE -- >85.2% dermatological and 74.1% gastrointestinal, mainly. 26% withdrawal treatment.
- **Dabrafenib/cobimetinib**: median PFS 10.1 (IC95%:7.7-NA); median OS was not reached. Median duration of treatment: 198 (IR:73-632).
  - 94.7% AE --> 52.6% dermatological, 68.4% gastrointestinal and 57.9% low-grade fever/discomfort. 15.8% withdrawal treatment

<table>
<thead>
<tr>
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<th>Vemurafenib/cobimetinib</th>
<th>Dabrafenib/trametinib</th>
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</thead>
<tbody>
<tr>
<td>Complete response</td>
<td>14.8%</td>
<td>26.3%</td>
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<tr>
<td>Partial response</td>
<td>33.3%</td>
<td>26.3%</td>
</tr>
<tr>
<td>Stable disease</td>
<td>7.4%</td>
<td>15.8%</td>
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<tr>
<td>Progress</td>
<td>11.1%</td>
<td>15.8%</td>
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<tr>
<td>Not assessable</td>
<td>33.3%</td>
<td>15.8%</td>
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CONCLUSION:
- The effectiveness observed in our patients was slightly lower than that seen in the pivotal CT (COBRIM-b) in vemurafenib/cobimetinib patients. It was similar to that seen in pivotal CTs (COMBI-v and COMBI-d) in patients treated with dabrafenib/trametinib.
  The toxicity profile of both drugs is similar to pivotal CTs’ results. Dabrafenib/trametinib was better tolerated than vemurafenib/cobimetinib.