INTRODUCTION

The fully human anti-EGFR monoclonal antibody panitumumab has demonstrated monotherapy activity in patients with wild-type KRAS (wt) expressing mCRC.

Skin toxicities associated with EGFR inhibitors are important quality of life and treatment adherence issues.

This single-arm, phase II study (20060314) prospectively evaluated the relationship between KRAS status and management of adverse event (AE) severity for patients treated with first-line panitumumab and FOLFIRI.

Skin toxicity data (incidence, time to skin and subcutaneous toxicities and management strategies) are described here.

There were no recommendations for prophylactic or specific reactive skin treatments.

METHODS

- Panitumumab (8 mg/kg intravenous infusion [IV] on day 1 of a 14-day cycle).
- No panitumumab-specific premedications were required before administration.
- FOLFIRI regimen (Irinotecan 180 mg/m² IV bolus on day 1, 5-FU 2250 mg/m² IV bolus on day 1, 5-FU 2250 mg/m² IV bolus over 46 hours on day 2, and atracurium before administration).

STUDY DESIGN

- Start of study: August 2006 - August 2007
- First dose of study drug: September 2006
- Last dose of study drug: January 2008

RESULTS

Baseline Patient Demographics and Disease Characteristics (Primary Analysis Set)

PANITUMUMAB + FOLFIRI (n = 145)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>wt (n = 85)</th>
<th>mt (n = 57)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, female</td>
<td>57 (67.1)</td>
<td>33 (58)</td>
</tr>
<tr>
<td>Age – years, median (min, max)</td>
<td>63 (21, 84)</td>
<td>65 (37, 80)</td>
</tr>
<tr>
<td>ECOG performance status 0–2</td>
<td>96 (91)</td>
<td>92 (16)</td>
</tr>
<tr>
<td>Prior anti-cancer therapy</td>
<td>60 (50)</td>
<td>35 (59)</td>
</tr>
<tr>
<td>Sites of metastatic disease</td>
<td>18 (21)</td>
<td>15 (24)</td>
</tr>
<tr>
<td>Liver only</td>
<td>36 (42)</td>
<td>27 (44)</td>
</tr>
<tr>
<td>Liver plus other sites</td>
<td>48 (58)</td>
<td>47 (77)</td>
</tr>
<tr>
<td>Other sites only</td>
<td>16 (21)</td>
<td>25 (42)</td>
</tr>
</tbody>
</table>

Skin, Nail and Ocular Toxicities

- Median duration of therapy was 6.9 months in the wt strata and 5.8 months in the mt strata.
- Any grade skin, nail and ocular toxicities occurred in 151 patients (98%) of the overall population (grade 3/4 in 58 patients [39%]).
- Grade 3/4 toxicities were observed in 34% and 31% in patients in wt and mt strata, respectively.
- In the wt and mt strata, respectively:
  - Median time to first toxicity was 8 days (min 0, max 155) and 10 days (min 0, max 125).
  - Median time to resolution of toxicity after last dose panitumumab was 108 days (min 0, max 350) and 71 days (min 5, max 102).
  - Median duration of toxicity was 402 days (min 14, max 492) and 321 days (min 18, max 443).

Skin Toxicity by KRAS wt and mt strata, respectively

- Grade 3 toxicities were reported in 25% and 22% of patients in wt and mt strata.
- Grade 4 toxicities were reported in 7% and 2% of patients in wt and mt strata.

Management of Dermatological and Nail Toxicities

- Some of the last patients enrolled in this trial may have received prophylactic skin toxicity treatment.
- In other institutes, patients received reactive topical skin toxicity treatment, initiated as required at incidence.
- Some of the last patients enrolled in this trial may have received prophylactic skin toxicity treatment based on prophylactic skin toxicity treatment practiced in other institutes.

Medications Used For Treatment and Management of Skin or Nail Toxicities

- Oral antibiotics are incorporated into the management strategy for patients with severe acneiform dermatitis.

CONCLUSIONS

- Combining panitumumab with first-line FOLFIRI appears to be well-tolerated.
- Skin toxicities observed when panitumumab is used in combination with FOLFIRI are similar to those observed with panitumumab monotherapy.
- Skin and cutaneous toxicities appear to be consistent across both KRAS groups.

REFERENCES


ACKNOWLEDGEMENTS

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