NSCLC, metastatic

PROPHYLACTIC TREATMENT FOR RASH INDUCED BY EGFR INHIBITOR IMPROVES RASH WITHOUT COMPROMISING ON EFFICACY THE PANCANADIAN RASH TRIAL: A RANDOMIZED PHASE III TRIAL IN NSCLC

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Aim: Erlotinib is approved for the treatment of patients with metastatic NSCLC following progression of chemotherapy as well for patients who harbour an EGFR mutation. Rash may limit exposure to drug and compromise efficacy. The objective of our study was to determine the proper treatment of EGFR inhibitor-induced rash in the 2nd or greater setting. A secondary objective was to prospectively observe the relationship between rash and survival and to see if intervention for rash was detrimental.

Methods: 150 patients metastatic NSCLC to be started on erlotinib in 2nd/3rd line were randomized to: Arm 1: Prophylactic: Minocycline (150 po bid 4 weeks) on day 1 of erlotinib Arm 2: Reactive: Topical clindamycin plus hydrocortisone +/- minocycline upon rash occurrence Arm 3: Control: No treatment of rash unless severe (Grade 3)

Results: Although not statistically significant, previous results showed Arms 1 and 2 had the longest overall survival from randomization. Arm 1: 7.6 months, Arm 2: 8.0 months, Arm 3: 6.0 months p = 0.38 Median survival was analyzed for the 150 patients for worst grade of rash experienced. Survival was significantly longer in patients who experienced severe or moderate rash (Grade 3 or 2) versus mild or no rash (Grade 0/1). Grade 3 rash: 11.4 months, Grade 2 rash: 10.1 months, Grade0/1 rash: 5.5 months p = 0.0093 Porphylactic minocycline in Arm 1 increased Grade 2 and decreased Grade 3 rash significantly. p= 0.3.

Table: 1277P Number and Percent of Patients with Worst Rash Grade for each Treatment Arm

<table>
<thead>
<tr>
<th>Arm</th>
<th>Rash Grade 0/1 N%</th>
<th>Rash Grade 2 N%</th>
<th>Rash Grade 3 N%</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>25 (50%)</td>
<td>20 (40%)</td>
<td>5 (9.5%)</td>
<td>50</td>
</tr>
<tr>
<td>2</td>
<td>28 (46%)</td>
<td>15 (30%)</td>
<td>7 (14.3%)</td>
<td>50</td>
</tr>
<tr>
<td>3</td>
<td>28 (46%)</td>
<td>5 (10%)</td>
<td>17 (34.1%)</td>
<td>50</td>
</tr>
</tbody>
</table>

Conclusions: In this prospective trial, a relationship between severity of rash and survival was seen. Moderate (Grade2) and severe (Grade3) rash demonstrated a superior overall survival compared to no or mild (Grade 1) rash. Prophylactic minocycline reduced the incidence of severe Grade 3 rash but increased the moderate Grade2 rash. Prophylactic minocycline should be considered in patients upon initiation of erlotinib therapy.

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