An open-label single-arm, phase II trial of zalutumumab, a human monoclonal anti-EGFR antibody, in patients with platinum-refractory squamous cell carcinoma of the head and neck.

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Introduction:

Treatment for patients with platinum-refractory metastatic SCCHN is limited. Cetuximab has been approved in the US for platinum-refractory SCCHN patients based on a phase II trial that demonstrated 13% RR and median OS of 5.9 months. Recently a phase III trial of zalutumumab, a human monoclonal IgG1k antibody against EGFR, showed significant increase in PFS versus best supportive care (Hx-EGFr-202). Here, we present the results of a companion phase II trial in patients with platinum-refractory R/M SCCHN.

Objectives:

- Primary objective: OS of platinum-refractory R/M SCCHN patients treated with zalutumumab + BSC.
- Secondary objectives: PFS, efficacy, safety.

Methods:

- Inclusion criteria: patients with platinum-refractory R/M SCCHN, WHO PS 0-2 and adequate organ function.
- Exclusion critieria: chemotherapy < 4 weeks from planned initiation of treatment.
- Patients received weekly infusions of zalutumumab individually titrated to a grade 2 skin rash (**Fig.1**) until PD, patient's decision to withdraw or unacceptable toxicity.
- The analysis was based on the intent-to-treat principle and OS was estimated using the Kaplan-Meier method.

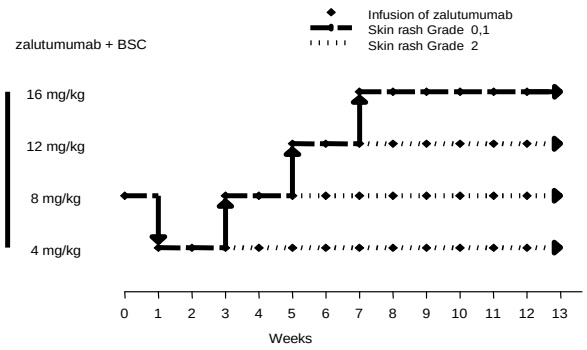

Fig. 1. Zalutumumab Dose Titration Scheme.

Results:

- 90 patients were enrolled. Patient characteristics are shown in **Table 1**.
- Median OS was 5.3 months (95% CI [4.1, 7.1]) (**Fig. 2**). Summarized efficacy results are shown in **Table 2**.

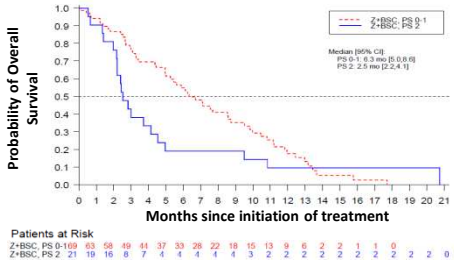

Fig.2. Kaplan-Meier curve of OS in zalutumumab-treated platinum-refractory R/M SCCHN patients.

- A summary of AEs related to zalutumab is shown in **Table 3**. 74% of patients had expected skin rash.
- 76 patients (84%) died during the study and the majority (59%) of deaths were due to disease progression. 2 deaths were deemed related to zalutumumab (cardiac arrest, respiratory acidosis).

Table 1. Baseline Patient Characteristics.

Characteristic	Zalutumumab + BSC (n=90)
Age (years)	
Median	59 (38-81)
<65	70 (78%)
>=65	20 (22%)
Sex	
Women	18 (20%)
Men	72 (80%)
Median disease duration (months)	
<=24	55 (61%)
>24	35 (39%)
WHO Performance Status	
PS 0	22 (24%)
PS 1	47 (52%)
PS 2	21 (23%)
Distant metastasis	
No	23 (26%)
Yes	67 (74%)

Table 2. Summarized Efficacy Results.

Endpoint	Zalutumumab + BSC (n=90)
OS	5.3 months (95% CI [4.1, 7.1])
PFS	2.15 months (95% CI [2.0, 2.6])
ORR	5.7%
CR	1%
PR	5%
DCR	39.8%

Table 3. Summary of Adverse Events Related to Zalutumumab.

	Zalutumumab + BSC N=90	
	All	Grade 3-4
Total	79 (88%)	17 (19%)
Rash	67 (74%)	4 (4%)
Hypomagnesemia	21 (23%)	4 (4%)
Pyrexia	13 (14%)	1 (1%)
Skin fissures	12 (13%)	NR
Fatigue	10 (11%)	1 (1%)
Pruritus	9 (10%)	NR
Vomiting	9 (10%)	1 (1%)
Nausea	8 (9%)	2 (2%)
Mucosal inflammation	7 (8%)	NR
Asthenia	7 (8%)	NR
Paronychia	7 (8%)	NR
Diarrhea	6 (7%)	NR
Headache	6 (7%)	1 (1%)
Folliculitis	5 (6%)	NR
Hypokaliemia	1(1%)	1 (1%)
Oral pain	1 (1%)	1 (1%)
Pneumonitis	1 (1%)	1 (1%)
Respir. tract infection	1 (1%)	1 (1%)

Conclusions:

- This study supported the results of the Hx-EGFr-202 trial and showed reasonable efficacy of zalutumumab in highly treated, chemotherapy-resistant patients with R/M SCCHN.
- Dose titration by skin rash was safe and feasible.
- The toxicity profile was consistent with that of approved EGFR monoclonal antibodies.

References:

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