Anti-EGFR-immunoliposomes loaded with doxorubicin in patients with advanced triple-negative, EGFR positive breast cancer – A multicenter single arm phase II trial (SAKK 24/14)

Andreas Wicki[1]*, Christoph Mamot[2]*, Ursula Hasler-Strub[3], Salome Riniker[3], Qiyu Li[4], Lisa Holer[4], Daniela Bärtschi[4], Khalil Zaman[5], Roger von Moos[6], Konstantin J. Dedes[1], Urban Novak[7], Alexandre Bodmer[8], Reto Ritschard[9], Ellen C. Obermann[10], Véronique Membrez-Antonioli[11], Ursina Zürrer[12], Clemens Caspar[13], Christoph Rochlitz[9#], Ralph Winterhalder[10#]
for the Swiss Group of Clinical Cancer Research (SAKK)

SAKK
WE BRING PROGRESS TO CANCER CARE

e-poster #268P

Affiliations: [1]University Hospital and University of Zurich, Zurich, Switzerland, [2]Cantonal Hospital Aarau, Aarau, Switzerland, [3]Cantonal Hospital St. Gallen, St. Gallen, Switzerland, [4]Swiss Group for Clinical Cancer Research (SAKK) Coordinating Center, Bern, Switzerland, [5]Lausanne University Hospital CHUV, Lausanne, Switzerland, [6]Cantonal Hospital Graubünden, Chur, Switzerland, [7]Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, [8]University Hospital Geneva, Geneva, Switzerland, [9]University Hospital Basel, Basel, Switzerland, [10]Cantonal Hospital Lucerne, Lucerne, Switzerland, [11]Hôpital du Valais, Hôpital de Sion, Sion, Switzerland, [12]Cantonal Hospital Winterthur, Winterthur, Switzerland, [13]Cantonal Hospital Baden, Baden, Switzerland, *shared first authorship #shared last authorship

Background

Advanced triple negative breast cancer (TNBC) is a highly chemo-sensitive disease displaying a dismal short-term prognosis with more than three quarters of patients in progression 12 months after the initiation of conventional chemotherapy. Approximately 2/3 of TNBC are expressing EGFR. Breast cancer, including TNBC, is a disease highly sensitive to anthracylines. We have developed an anti-EGFR targeted nanocontainer drug by inserting anti-EGFR antibody fragments into the membrane of pegylated liposomes (anti-EGFR-ILs-dox). The payload consists of doxorubicin, a standard drug for breast cancer, including TNBC. Data from a phase I trial[1], in 26 patients with different solid tumors, shows low toxicity and some signs of efficacy of anti-EGFR-IL-dox.

Study design

Prospective, proof-of-concept, open-label, one-arm, multicenter phase II trial.
48 patients, whose cancer expressed EGFR by immuno-histochemistry assessed centrally, were treated with anti-EGFR-ILs-dox 50 mg/m^2 i.v., on day one of a 28 days cycle until progression. The primary endpoint was progression-free survival at 12 months (PFS12m). For the statistical analysis, we tested the null hypothesis PFS12m ≤25% against the alternative hypothesis PFS12m ≥40%. The reference for the PFS12m of 25% for the null hypothesis was the TNBC subgroup of the ATHENA trial[2].

Acknowledgements:
The trial was supported by Merrimack and research agreements with the following institutions: Swiss State Secretary for Education, Research and Innovation (SERI), Swiss Cancer Research Foundation (SCS) and Swiss Cancer League (SCL) and a grant by The Rising Tide Foundation.

Results

The Kaplan-Meier estimate for PFS12m was 13% (95% CI: 5-25%). The median PFS was 3.5 months (95% CI: 1.9-5.4). Thus, the trial has not reached its primary endpoint. The observed PFS12m is comparable to the one observed in a trial with Nab-paclitaxel in TNBC (17.7%).

The **primary endpoint** of the trial is:

- Progression-free survival at 12 months

Secondary endpoints of the trial are:

- Objective response rate
- Duration of response
- Time to progression
- Progression-free survival
- Overall survival
- Adverse events

Variable	Total (N=48)
Progression-free survival rate at 12 months	13%
One-sided 90% CI (lower bound)	7%
Two-sided 95% CI	(5%, 25%)

Tab. 1: Primary endpoint

Over the whole course of therapy, treatment-related grade 1, 2, 3 and 4 AEs were observed in 18.8%, 25.0%, 31.3% and 8.3% of the patients, respectively.

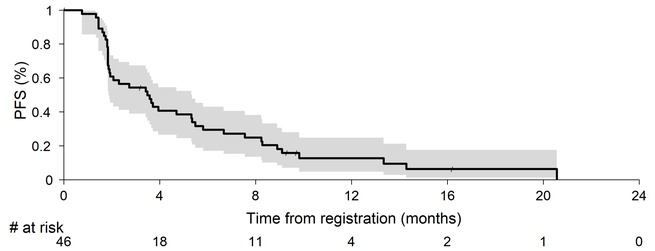

Fig. 1: PFS in the full analysis set.

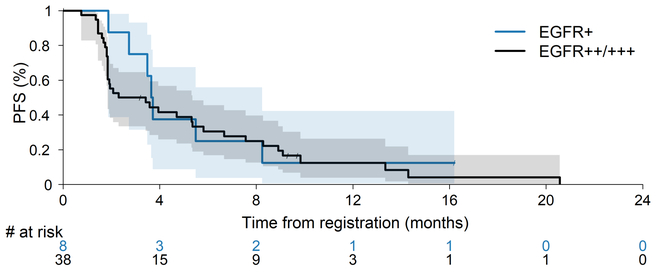

Fig. 2: PFS according to EGFR expression (IHC).

Conclusion

Based on these results, anti-EGFR-ILs-dox should not be further developed for TNBC. It remains an open question whether anti-EGFR-ILs-dox would offer more opportunities in other EGFR-expressing malignancies, where targeting EGFR has already shown anticancer effects.

References

[1] Mamot C, Ritschard R, Wicki A, et al., Lancet Oncology, 2012, 13:1234-41
[2] Smith I, Pierga JY, Biganzoli L, et al., Breast Cancer Res Treat, 2011, 130:133-143