Cetuximab-related skin toxicity (Cet-ST) in metastatic colorectal cancer (mCRC) patients and its correlation with molecular markers: Results from the German AIO CRC-0104 trial

**Design**
- **Background:** Skin toxicity is a frequent adverse event of EGFR targeting agents. The role of cetuximab-related skin toxicity (Cet-ST), for the most acidifing skin rash, as a prognostic or predictive factor of treatment efficacy is currently under discussion.

**Methods:**
- **Polymorphism and clinical data analysis:** EGFR intron-1 CA repeat (CA-SSR) and KRAS codon-12 mutant tumors were investigated in tumor specimens of metastatic colorectal cancer (mCRC) patients treated with Cetuximab plus FOLFIRI (CAPIRI) or oxaliplatin plus capecitabine plus irinotecan (CAPOX) as first-line chemotherapy (AIO CRC-0104). Correlation of Cet-ST was assessed with EGFR intron-1 CA repeat (CA-SSR) and KRAS codon-12 mutant tumors.

**Results:**
- **Correlation with EGFR intron-1 CA repeat (CA-SSR):** EGFR intron-1 CA repeat (CA-SSR) appears to be a predictor of Cet-ST. The mean time of occurrence of Cet-ST was longer in patients with Cet-ST grade 2-3 than in patients with grade 0-1 Cet-ST (13.6 vs. 8.9 days, p < 0.001).

**Discussion:**
- **Skin toxicity and response:** Skin toxicity is a frequent adverse event of EGFR targeting agents. The role of Cet-ST, for the most acidifing skin rash, as a prognostic or predictive factor of treatment efficacy is currently under discussion.
- **Survival analysis:** The prognostic and predictive value of Cet-ST in relation to treatment response and survival of patients of a randomized trial investigating CAPIRI plus cetuximab versus CAPOX plus cetuximab as first-line treatment of mCRC was analyzed. Cet-ST and were used for this analysis. Overall response rate was higher in patients with Cet-ST grade 2-3 than in patients with grade 0-1 Cet-ST (62.1% vs. 41.3%).

**Conclusions:**
- Cetuximab-related skin toxicity (mostly acneform rash) is a strong predictor of outcome.
- First-cycle rash predicts favourable outcome.
- Cet-ST appears to be neither a prognostic nor a predictive factor since this effect is more evident in patients with KRAS codon-12 mutant tumors.
- EGFR intron-1 polymorphism appears to be a predictor of Cet-ST.