Aim: MC (continuous administration of low doses of conventional chemotherapeutics) is characterized by an excellent therapeutic index. In fact, we recently demonstrated that 24% of patients with ABC receiving daily dalteparin and oral cyclophosphamide, twice-weekly methotrexate, and daily prednisone (dalCMP) achieved clinical benefit with minimal toxicity. While there are no predictive markers of response to MC, circulating miRNAs have a high potential to serve as easy accessible biomarkers. Hence we sought to generate a predictive plasma miRNA signature of response to dalCMP.

Methods: We analyzed pre-treatment plasma samples from top-responders versus patients with dalCMP refractory ABC (n = 6 each) using the nCounter® miRNA expression assay (NanoString Technologies). Candidate miRNAs were validated by qRT-PCR.

Results: Of 800 human miRNAs of miRBase v18.0, we identified 210 miRNAs expressed in all patient samples. Of these, the average expression of 24 miRNAs displayed a > 2-fold change in either direction in responders to dalCMP (mean ± SD time to tumor progression 65.6 ± 13.9 weeks) versus non-responders (3.2 ± 1.0 weeks). Student t-testing followed by Benjamini–Hochberg correction revealed 6 miRNAs significantly upregulated in non-responders: miR-451a, miR-122-5p, miR-142-3p, miR-548ai, miR-150-5p, and miR-342-3p. Using qRT-PCR, we confirmed the differential expression pattern of miR-451a, miR-122-5p, miR-142-3p, and miR-548ai. In contrast to our findings, miR-451a overexpression has been found by others to exert in vitro chemosensitizing properties, whereas miR-122-5p, miR-142-3p and miR-548ai have not been associated with chemosensitivity modulation to date.

Conclusions: We describe the first candidate miRNA signature predicting response to MC (i.e. dalCMP), currently being validated in the original and extension dalCMP study populations (n = 92). This signature may become a helpful tool to select patients with ABC suitable for dalCMP, and to possibly predict response to other MC regimens as well as to MC used for other tumor types.

Disclosure: All authors have declared no conflicts of interest.