# 2310 28-Day Metronomic Therapy for Relapsed Refractory Multiple Myeloma

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## Background

The advent of novel therapies has led to tremendous progress in the treatment of multiple myeloma (MM). However, management of patients with high-risk disease who have failed approved agents and have rapidly progressive disease with cytopenias continues to be challenging. While palliative care is an option, many patients hope to qualify for a clinical trial option. Here we report results of a 28-day metronomic therapy (METRO-28) consisting of continuous administration of very low doses of classical chemotherapeutic agents. Sixteen-day cycles of metronomic therapy were previously shown to have a favorable response with acceptable toxicity profiles in MM patients (Papanikolaou *et al*. Haematologica 2013).

## Aim

To investigate the efficacy and toxicity in patients with high-risk relapsed refractory MM (RRMM) ineligible for clinical trial options receiving 1 cycle of METRO-28.

## Method

We retrospectively analyzed the clinical outcomes of 106 RRMM, treated with 1 cycle of 28-day metronomic chemotherapy at the Tisch Cancer Institute – The Mount Sinai Hospital. METRO-28 consists of 6 agents: dexamethasone 8 mg on days 1 through 4, 7 through 10, 13 through 16, 19 through 22 and 25 through 28; bortezomib 1 mg/m$^2$ on days 1, 4, 7, 10, 13, 16, 19, 22, 25, 28; cisplatin 1 mg/m$^2$ daily; doxorubicin 1 mg/m$^2$ daily; thalidomide 100 mg daily; and vincristine flat dose 0.06 mg daily. METRO-28 was administered through a central line in either the inpatient or outpatient setting.

## Result

Our cohort of 106 RRMM patients has a median age of 65 years (range: 35-85) and at a median of 59 months from time of diagnosis; 42% were females. They had a median of 7 prior lines of therapy (range: 1 - 25); with 73% triple- and 58% penta-refractory cases. Prior autologous transplantation was utilized in 69% of patients including tandem transplants in 30%. Moreover, 78% of patients carried high-risk cytogenetic features, including 1q21 duplication/amplification (89%), 17p deletion (49%), t(4;14) (17%), t(14;16) (17%) or t(14;20) (3%).

At the time of METRO-28 initiation, patients were cytopenic with grade 3 and 4 anemia (21%), neutropenia (8%) and thrombocytopenia (23%). Profound cytopenias in some patients led to early discontinuation of treatment; forty-three patients (41%) received the full 28-day course of METRO-28, while 11%, 17%, 20% and 11% were treated for <1 week, <2 weeks, <3 weeks or <4 weeks, respectively. Grade 3-4 cytopenia increased: anemia 66%, leucopenia 61%, neutropenia 55% and thrombocytopenia 76%.

On an intent to treat basis (106 patients), the deepest response included 2% stringent complete response (sCR), 7% near complete response (nCR), 7% very good partial response (VGPR), 28% partial response (PR), 11% minimal response (MR) and 12% stable disease (SD). Only 43 patients (41%) completed all 4 weeks of METRO-28 and had a 72% overall response rate (ORR) and 88% clinical benefit rate (CBR). Seventy-four percent of these patients were able to move on to new therapies, including novel agents and clinical trials. Their overall survival (OS) was 11.8 months (range: 6.1-NE) as opposed to an OS of 4.2 months (range: 3.4-7.2) for patients with <4 weeks of METRO-28. Sixty-three patients had their treatment interrupted: 34 due to disease progression or absence of response, 18 due to bacterial or viral infections and 11 due to hematologic toxicity.

## Conclusion

Giving 1 cycle of METRO-28 is better tolerated in patients with good hematologic reserve and offers an opportunity for a clinical benefit and a bridge to a subsequent treatment option for these advanced refractory myeloma patients.