

Effect of TM-mediated Copper depletion on High-risk breast cancer relapse and the Tumor microenvironment

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INTRODUCTION

- Cancer progression and metastasis requires the coordination of numerous cellular and molecular factors that ensure tumor cell survival, migration, motility and colonization of distant sites
- Copper functions as a co-factor for a host of these proteins, such as the matrix metalloproteinases that allow degradation and remodeling of the extracellular matrix
- Tetrathiomolybdate (TM) is a copper chelator used to treat Wilson's disease
- Studies have shown TM's stabilizing effect on cancer progression

AIMS

- **To illicit the effect of TM-mediated Copper depletion on cellular and molecular factors involved in cancer progression and metastasis.**

METHODS

Breast cancer at high risk of relapse and NED
N= 75

Daily oral TM For 2 years to achieve Cp target ≤ 17 mg/dL

Primary endpoint:
- VEGFR2+ EPCs
Secondary endpoints:
- Progression-Free Survival
- Overall Survival
- VEGFR1+ HPCs
- Adverse events
- Circulating markers in the tumor microenvironment

High Risk
➢ Stage III and IV NED breast cancer
➢ Stage II TNBC

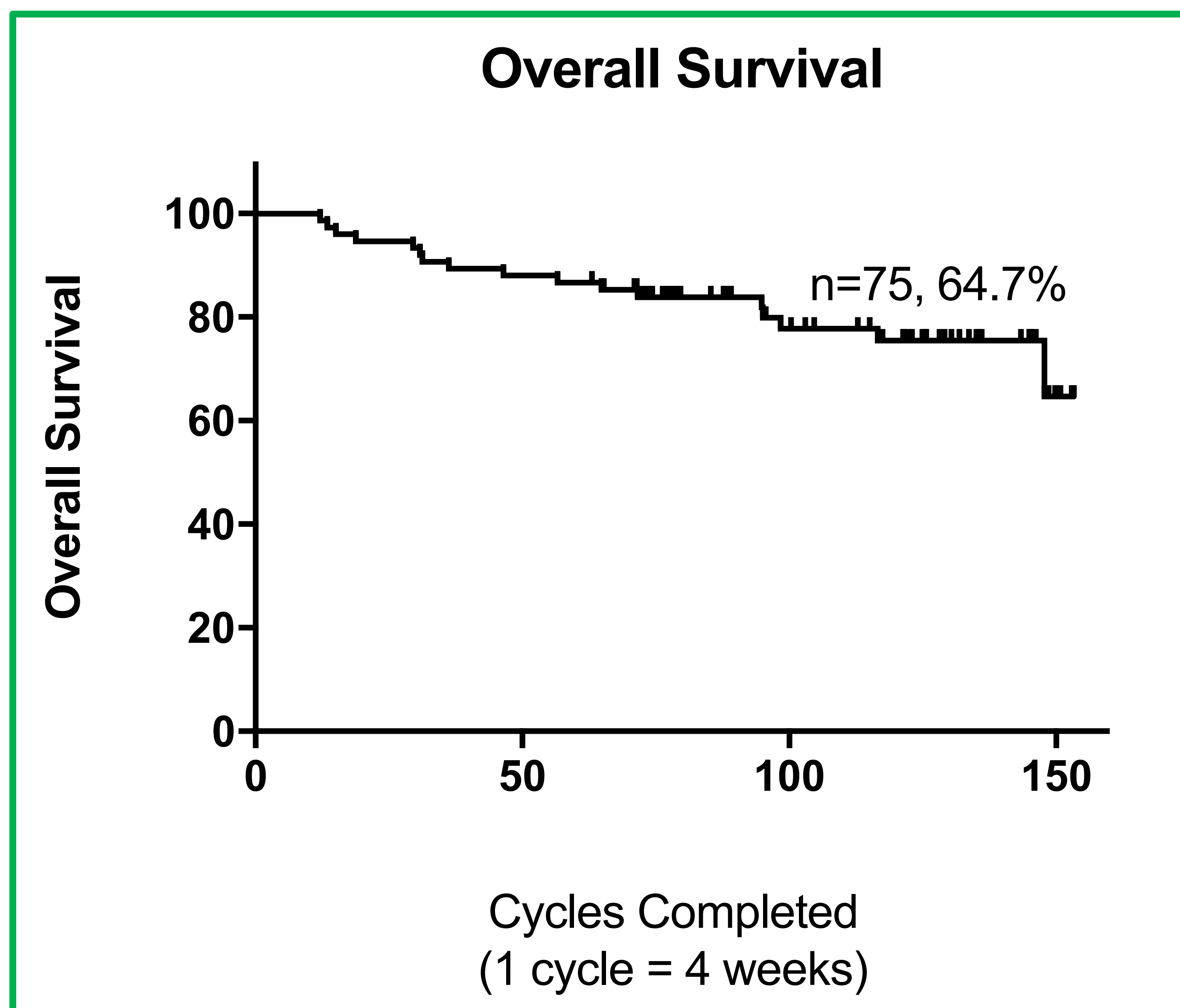
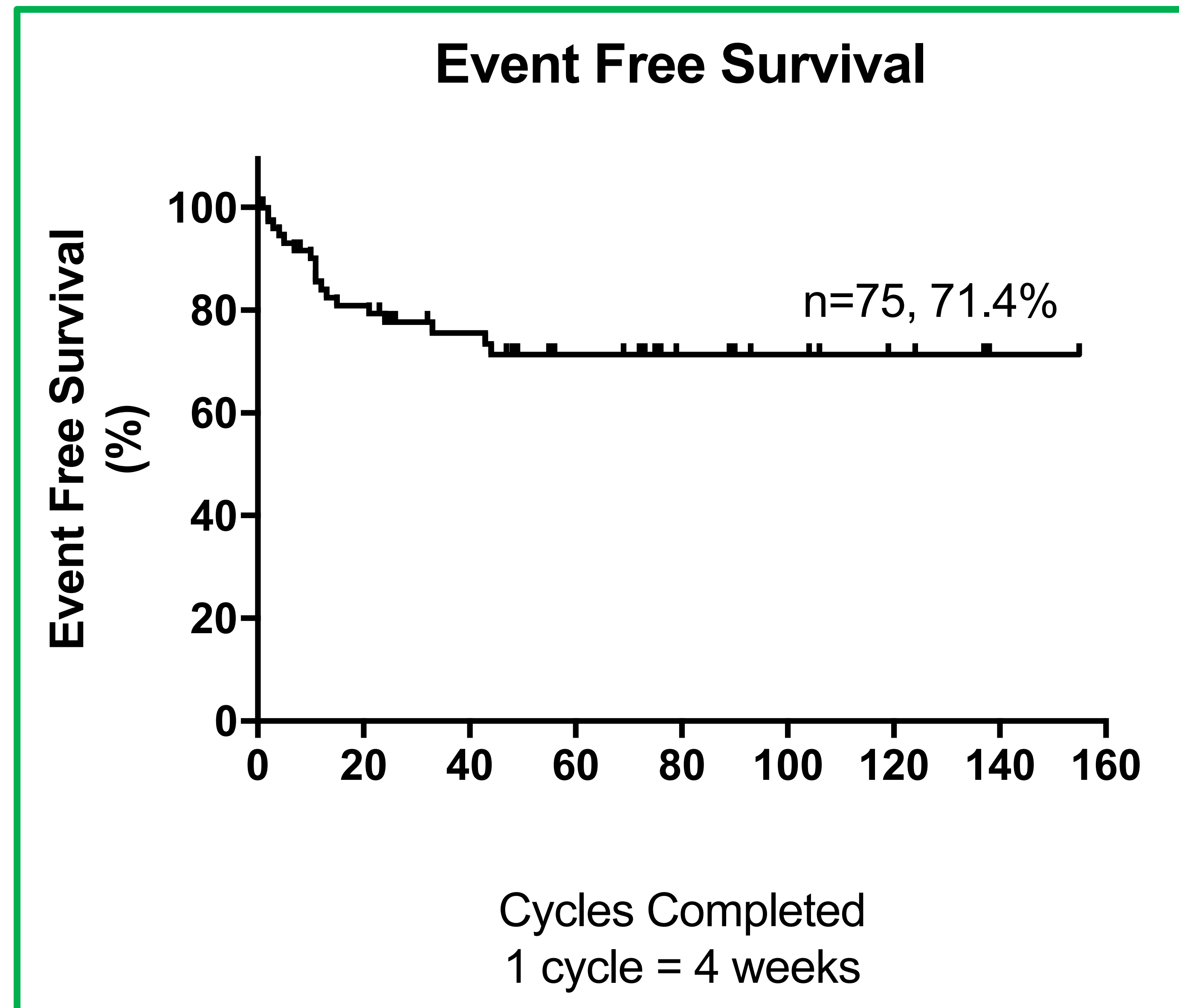
No Evidence of disease (NED)
➢ Physical exam
➢ Labs: CBC, CMP, tumor markers
➢ Imaging: CT scan with bone scan or PET/CT scans

Local and systemic therapy:
➢ Completion of standard therapy

Once every 4 weeks (1 cycle)
➢ Physical exam
➢ CBC, CMP, tumor markers
➢ Ceruloplasmin (Cp) level
➢ Flow cytometry for BMD progenitors and other research blood (banked)

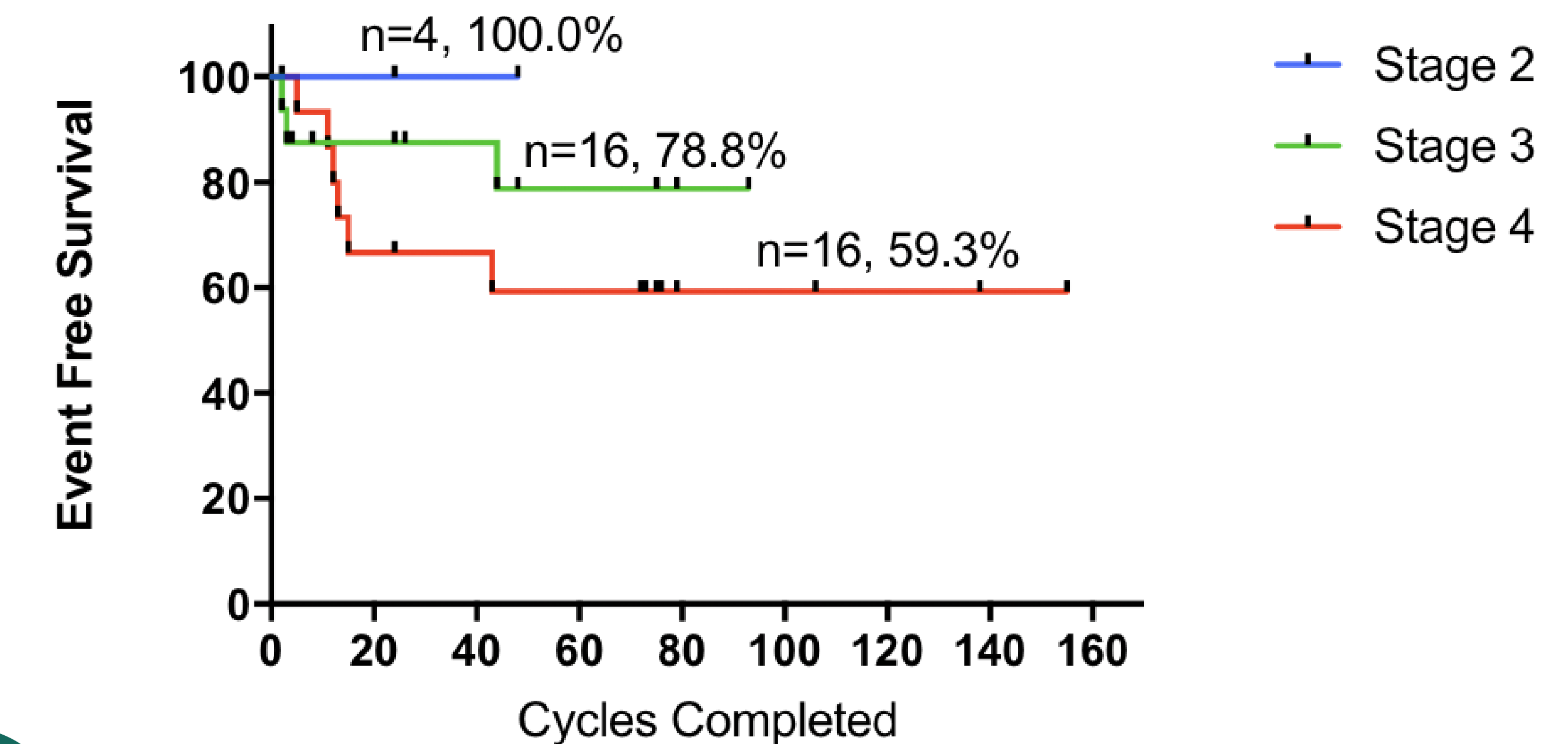
Once every six months
➢ CT with BS or PET/CT

RESULTS



RESULTS

EFS of Triple Negative Patients by Stage (n=36)



DISCUSSION

- Copper depletion using TM increases event free survival and overall survival in both TNBC and other high risk breast cancers.
- The exact mechanisms underlying the benefits of Cu depletion in the tumor microenvironment are still not well understood

FUTURE DIRECTIONS

- Analyzing different parameters affected by Cu depletion in patients that relapse vs controls.
- The effect of Cu depletion on cytokines and matrix metalloproteases
- Analyzing the effect on VEGFR2 +EPCs, and markers for Collagen degradation (C1M) and formation (Pro-C3)

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