

1148226 - Intervention to hepatic and pulmonary METastases in breast cancer patients: Prospective, multi-institutional registry study-IMET; Protocol MF 14-02

Atila Soran¹, Serdar Ozbas², Beyza Ozcinar³, Arda Isik⁴, Lutfi Dogan⁵, Kazim Senol⁶, Ahmet Dag⁷, Hasan Karanlik⁸, Ozgur Aytac⁹, Guldeniz Karadeniz Cakmak¹⁰, Kubilay Dalci¹¹, Mutlu Dogan⁵, Yavuz Atakan Sezer¹², Mustafa Sehsuvar Gokgoz⁶, Enis Ozyar¹³, Efe Sezgin¹⁴, Breast Health Working Group International.

¹University of Pittsburgh, Department of Surgery, Pittsburg, PA, ²Ankara Guven Hospital, Department of Surgery, Ankara, Turkey, ³Istanbul University, Istanbul Faculty of Medicine, Department of Surgery, Istanbul, Turkey, ⁴Medeniyet University, Department of Surgery, Istanbul, Turkey, ⁵Ankara Oncology Hospital, Department of Surgery, Ankara, Turkey, ⁶Uludag University Faculty of Medicine, Department of Surgery, Bursa, Turkey, ⁷Mersin University, Faculty of Medicine, Department of Surgery, Mersin, Turkey, ⁸Istanbul University, Institute of Oncology, Istanbul, Turkey, ⁹Baskent University, Department of Surgery, Adana, Turkey, ¹⁰Zonguldak Bulent Ecevit University, Department of Surgery, Zonguldak, Turkey, ¹¹Cukurova University, Department of Surgery, Adana, Turkey, ¹²Trakya University, Department of Surgery, Edirne, Turkey, ¹³Acibadem Hospital, Department of Radiation Oncology, Istanbul, Turkey, ¹⁴Izmir Institute of Technology, Faculty of Engineering, Izmir, Turkey.

Background/Objective: One-fourth of early-stage breast cancer (BC) becomes metastatic at follow-up. Limited metastases represents a clinical state of metastatic disease that is limited in the number of metastatic sites and extent of disease, and amenable to metastasis-directed intervention. The aim of this prospective study is to evaluate intervention to limited metastases in lung and/or liver.

Methods: Luminal A/B and/or HER-2 neu (+) patients with operable lung and/or liver metastases in follow-up after primary BC treatment is completed, and patients who were diagnosed with metastasis after 2014 were included in the study. Demographic, clinical, tumor-specific data, and metastasis detection-free interval (MDFI) were collected. Bone metastasis, in addition to lung and liver metastases, were also included the analysis. Patients were divided into 2 groups according to the treatment modality to metastases - either systemic therapy only (ST) or intervention (IT). The characteristics of the patients were compared with X2 test. Overall survival curves were calculated according to the Kaplan-Meier (KM) (log-rank) method. A multivariable analysis was performed by Cox regression. Statistical significance was defined as a p-value <0.05.

Results: Two hundred patients were enrolled until June 2020. Demographic data were similar between the groups; median follow-up time was 77 (range:55-107) months in IT group (n= 119; 59.5%) and 57 (range:39-84) months in ST group (n=81; 40.5%). Median MDFI was 40 (range:23-70) months and 35 (range:13-61) months, respectively in IT and ST groups (p=0.47). The groups had similar primary tumor and axillary surgery; the majority of them (74%) had axillary lymph node dissection. The majority of the patients had liver metastasis (n=116, 58.0%), and 101 (50.5%) of patients had lung metastases; 17 (8.5%) patients had both lung and liver metastases. Primary tumor was ER/ PR (+) in 150 (75.0%) patients and 64 (32.0%) patients had HER2 neu (+) tumors. Metastatic site surgical resection was done in 64 (32.0%) patients, and 55 (27.5%) patients underwent metastatic ablative interventions. In KM survival analysis, hazard of death (HoD) was 56% lower in the IT group than ST group (HR 0.44: 95% CI 0.44; 0.26-0.72; p=0.001). The HoD was lower in the IT group than ST group regarding age <55 (HR 0.32: 95% CI 0.17-0.62; p=0.0007). In the multivariable cox regression model, HoD was significantly lower in patients who underwent intervention to metastases and who had MDFI >24 months compared to no intervention group and shorter MDFI, but having liver metastases increases the HoD 2 times compared to lung metastases (Table).

Conclusions: Metastasis-directed interventions have reduced the risk of death in patients with limited lung/liver metastases who are amenable to interventions after primary cancer treatment is completed. In the selected group of patients such as luminal A/B, HER2 neu (+) BC, younger than 55 years old, limited metastases to lung and/or liver, and MDFI >24 months, surgical or ablative therapy to metastases should be considered and discussed in the tumor boards.

Table. Univariate and multivariable Cox models for overall survival.

Parameter	HR (95%CI)	p	HR _{adj} (95%CI)	P _{adj}
Metastasis intervention	0.44 (0.26-0.72)	0.001	0.39 (0.23-0.67)	0.0007
MDFI>24 months	0.20 (0.10-0.37)	<0.0001	0.17 (0.09-0.34)	<0.0001
Age <55	0.92 (0.55-1.56)	0.77	—	—
Pre-menopause	1.09 (0.64-1.77)	0.80	—	—
ER/PR (+)	1.46 (0.74-2.88)	0.28	—	—
Her2 neu (+)	0.94 (0.54-1.65)	0.84	—	—
Primary Breast surgery				
Segmental mastectomy	REF	—		
Mastectomy	0.98 (0.58-1.65)	0.94	—	—
Metastasized site				
Lung	REF	—	REF	—
Liver	1.98 (1.03-3.83)	0.04	2.07 (1.05-4.06)	0.03
Lung+ Bone	1.11 (0.26-4.83)	0.89	1.16 (0.27-5.10)	0.84
Liver+Bone	2.14 (1.08-4.22)	0.03	2.26 (1.12-4.57)	0.02
Multiple	1.01 (0.40-2.55)	0.98	0.80 (0.31-2.07)	0.64
Lymph Node status				
N0	REF	—		
N1	0.63 (0.31-1.28)	0.21	—	—
N2	1.11 (0.54-2.33)	0.76	—	—
N3	1.59 (0.76-3.32)	0.22	—	—

HR_{adj}: Adjusted for variables that are significant in univariate models, MDFI: metastasis detection free interval

1138722 - A DCIS biosignature with a novel residual risk subtype identifies patients with varying risk and RT benefit among younger and high-grade DCIS patients

Julie Margenthaler¹, Frank Vicini², Chirag Shah³, Rachel Rabinovitch⁴, Mylin Torres⁵, Fredrik Wärnberg⁶, Sheila Weinmann⁷, G Bruce Mann⁸, Pat Whitworth⁹, Rakesh Patel¹⁰, Brian Czerniecki¹¹, Michael Leo⁷, Jess Savala¹², Karuna Mittal¹², Steven Shivers¹², Troy Bremer¹²

¹Washington University in St. Louis, St. Louis, MO, ²GenesisCare, Farmington Hills, MI, ³Cleveland Clinic Taussig Cancer Institute, Cleveland, OH, ⁴University of Colorado Cancer Center, Aurora, CO, ⁵Emory University Winship Cancer Institute, Atlanta, GA, ⁶Sahlgrenska Akademin, Göteborgs Universitet, Göteborg, Vastra Gotaland, Sweden, ⁷Kaiser Permanente Center for Health Research, Portland, OR, ⁸Royal Women's Hospital, Parkville, Victoria, Australia, ⁹Nashville Breast Center, Nashville, TN, ¹⁰Good Samaritan Hospital, Los Gatos, CA, ¹¹Moffitt Cancer Center, Tampa, FL, ¹²PreludeDx, Laguna Hills, CA

Background/Objective: High nuclear grade and young age (<50 years) are 2 clinicopathologic factors commonly used to make treatment decisions in patients with DCIS. However, randomized studies have failed to identify low-risk patients who did not benefit from radiation therapy (RT) after breast-