

LETTERS TO THE EDITOR

The impact of efficacy of receptor conversion on metastases directed therapies in liver metastases with breast cancer

Dear Editor,

In metastatic breast cancer (mBC), liver metastases are a frequent occurrence. The term “oligometastatic” is described as an intermediate state between localized and widespread, metastatic disease. This disease setting is potentially characterized by different tumor biology with a less aggressive behavior, thus still eligible to local approaches [1]. Franzese and colleagues in their retrospective study in which evaluated outcome and toxicity of mBC with liver oligometastases treated with metastases-directed therapies (MDT), including surgery, stereotactic body radiation therapy (SBRT) or thermal ablation (radiofrequency or microwaves) [2]. They reported that combination of systemic therapy with liver MDT in oligometastatic BC results in durable disease control in a significant proportion of patients. They concluded that tumor biology, prior treatment and extent of disease may be useful to guide decision to add MDT to standard therapy. However, the authors did not give detailed information about variation in hormone receptors and HER-2 status between primary and mBC. The discordance rate of estrogen receptor (ER), progesterone receptor (PR), and HER2 status in distant metastases has frequently been reported. The actual incidence of this phenomenon has not been strictly defined. A recent meta-analysis including 39 studies assessing receptor conversion from primary breast tumors to paired distant BC metastases showed that negative to positive conversion percentages were 21.5, 15.9,

and 9.5% for ER, PR, and HER2. Furthermore, PR discordance was higher in bone and liver metastases compared with central nervous system metastases [3]. However, the impact of efficacy of receptor conversion on MDT is not known yet in liver metastases with BC. This issue merits further investigation.

References

1. Zegarac M, Nikolic S, Gavrilovic D et al. Prognostic factors for longer disease free survival and overall survival after surgical resection of isolated liver metastasis from breast cancer. *J BUON* 2013;18:859-65.
2. Franzese C, Comito T, Viganò L et al. Liver metastases directed therapy in the management of oligometastatic breast cancer. *Clin Breast Cancer* 2020; 20: 480-6.
3. Schrijver WAME, Suijkerbuijk KPM, van Gils CH et al. Receptor Conversion in Distant Breast Cancer Metastases: A Systematic Review and Meta-analysis. *J Natl Cancer Inst* 2018;110:568-80.

Kadri Altundag

MKA Breast Cancer Clinic, Ankara, Turkey.

*Corresponding author: Kadri Altundag, MD.
Email: altundag66@yahoo.com*

A closer look at pulmonary carcinoid in a large breast cancer dataset

Dear Editor,

Pulmonary carcinoids (PCs) are more commonly diagnosed in women and are generally diagnosed in the fifth decade of life. Their etiology is not clearly known. Associations with other diseases or types of cancer might give us some information about shared risk factors [1]. Buikhuisen and colleagues [2] investigated the association between PCs and other primary malignancies for identifying risk factors. In a total of 2933 patients with PCs found 425 consecutive primary malignancies in 376 of them. Concomitant diagnoses in the first year mainly comprised lung (n=59) and renal cancer (n=14). Metachronous malignancies beyond the first year were most common for breast (n=50), colorectal (n=41),

prostate (n=32), and lung cancer (n=29). They concluded that concomitant diagnosis of PC with other cancers is common, reflecting surveillance diagnostics. Apart from MEN-1 family history, no shared risk factors could be identified. The authors did not mention characteristics of breast cancer patients with PCs. One study evaluated cases of multiple PCs diagnosed between 1992 and 2003 in patients with history of breast cancer identified through a search of the pathology files [2]. They identified 12 women with a history of breast cancer and biopsy-proven PCs. Only 3 women were smokers. The mean age at diagnosis of the breast cancer was 62.8 years. The breast cancer was invasive carcinoma in 10 cases (9 ductal and 1 lobular) and ductal carcinoma *in situ* and malignant phyllodes tumor in 1 case each. However, the authors did not describe

molecular subtypes of breast cancer. Among my 6803 breast cancer patients who were diagnosed between 2002-2020, I identified one case with PC. She is currently 44-year-old and had a diagnosis of PC in December 2006 and underwent right lung lobectomy. She is non-smoker. Left breast cancer was diagnosed in May 2009 and she had left modified radical mastectomy with T3N2M0 stage and her tumor was HER-2 3+ and hormone receptor negative. She received 4 cycles of doxorubicin+cyclophosphamide and 12 weeks of paclitaxel and 1 year of trastuzumab and adjuvant radiotherapy. She is still in remission after 11 years. In conclusion, consideration should be given to the association between PC and clinical and pathological characteristics of breast cancer.

References

1. Velinovic M, Jankovic R, Jovanovic D et al. Tumor char-

acteristics, expressions of ERCC1, Bax, p53, IGF1R, Bcl2, Bcl2/Bax and prognostic factors for overall survival in patients with lung carcinoid. *JBUON* 2019;24:256-66.

2. Buikhuisen WA, Steinbusch LC, Kodach LL et al. Risk of second primary malignancies among patients with carcinoid of the lung. *Lung Cancer* 2020;151:5-7.
3. Darvishian F, Ginsberg MS, Klimstra DS, Brogi E. Carcinoid tumorlets simulate pulmonary metastases in women with breast cancer. *Hum Pathol* 2006;37:839-44.

Kadri Altundag

MKA Breast Cancer Clinic, Ankara, Turkey.

Corresponding author: Kadri Altundag, MD.

Email: altundag66@yahoo.com

MicroRNAs in esophageal carcinoma

Dear Editor,

Esophageal squamous cell carcinoma (ESCC) represents an aggressive malignancy, and also a leading cause of cancer-related mortality worldwide. In fact, it demonstrates a less than 20% 5-year survival rate due to late diagnosis [1]. Gene expression profiles in ESCC patients include a variety of genetic biomarkers that should be useful for a molecular discrimination of patients regarding treatment strategies and prognosis. Micro-RNAs (miRNAs/miRs) are considered novel significant and most promising markers for discriminating patients based on their molecular characteristics. MiRs are short, non-coding RNAs consisting of 20-25 nucleotides located at intra- or inter-gene regions. Functional miRs mediate a positive regulation of posttranscriptional gene silencing. Their deregulation in cancer cells due to genetic (mutations, translocations), epigenetic (DNA hypermethylation of tumour suppressor genes, extensive genomic DNA hypomethylation, aberrant histone modification patterns) and transcriptional alterations leads to a loss of miRs-mediated repression of target mRNA. Interestingly, a biphasic role of miRs in cancers of different histogenetic origin has been confirmed [2]. Extensive molecular analyses based on miRs expression RT-PCR arrays discovered a variety of them to be deregulated in the corresponding analyzed ESCC tissues [3]. Among them, 28 were down- and 11 up-regulated. Most importantly miR-885-5p, miR-140-3p, miR-708, miR-639, and miR-596 were novel examples of deregulated miRNAs in ESCC. Interestingly, a set of 16 miRs was found to influence the expression of 195 genes. Another study group analyzed the miR-613 in ESCC. They observed that this specific miR marker demonstrated low expression in the corresponding malignant tissues, whereas an over-expression was observed in normal esophageal epithelia. Interestingly, glucose-6-phosphate dehydrogenase (G6PD) is a direct target of miR-613. Similarly, miR-613 activation led to a decreased mRNA and protein amount of G6PD, matrix metalloproteinase (MMP)-2 and MMP-9. Finally, they concluded that miR-613 targets G6PD to suppress ESCC cell migration and invasion through reduced MMP2 and MMP9 expression combined with STAT3 down-regulation [4]. Additionally, another molecular analysis focused on the

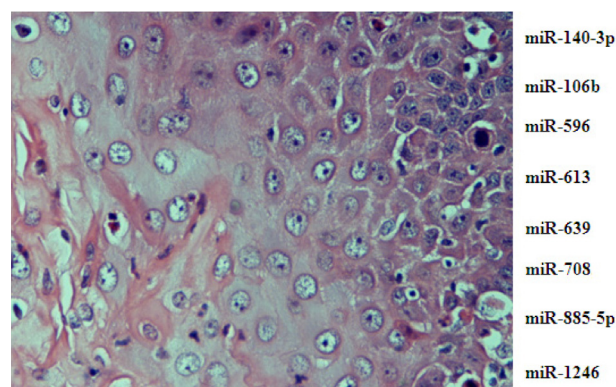


Figure 1. Histological image of a moderately differentiated (Grade 2) esophageal squamous cell carcinoma (ESCC) combined with a list of specific miRs that are frequently deregulated in this malignancy.

miR-1246 and miR-106b expression patterns in ESCC. Based on a serum microarray analysis of these miRs' expression, they observed miR-1246 increased and miR-106b decreased levels, respectively. They also reported a high miR-1246/miR-106b ratio correlated to a significant tumor invasion, progression, lymph node metastasis, and finally poor prognosis [5]. All of the previous novel genetic data based on miRs deregulation in ESCC show the importance of these genetic markers in understanding the different molecular signatures of the patients which modify response to therapeutic regimens and prognosis (Figure 1).

References

1. Jemal A, Siegel R, Xu J, Ward E. Cancer statistics, 2010. *CA Cancer J Clin.* 2010; 60:277-300.
2. Casalini P, Iorio MV. MicroRNAs and future therapeutic applications in cancer. *J BUON* 2009;14 (Suppl 1):S17-22.
3. Yang H, Su H, Hu N et al. Integrated analysis of genome-wide miRNAs and targeted gene expression

oesophageal squamous cell carcinoma (ESCC) and relation to prognosis. *BMC Cancer* 2020;20:388-402.

4. Su X, Gao C, Feng X, Jiang M. miR-613 suppresses migration and invasion in esophageal squamous cell carcinoma via the targeting of G6PD. *Exp Ther Med* 2020;19:3081-89.
5. Hoshino I, Ishige F, Iwatate Y et al. Usefulness of serum miR-1246/miR-106b ratio in patients with esophageal squamous cell carcinoma. *Oncol Lett* 2020;20:350-55.

Dimitrios Tsounis¹, Ioannis Stavrakis², Theodoros Niotis³, Evangelos Tsiambas⁴

¹Department of Gastroenterology, 251 Air Force Hospital, Athens, Greece; ²ENT Department, "Sotiria" General Hospital, Athens, Greece; ³2nd Department of Surgery, Aretaieion University Hospital, Athens, Greece; ⁴Department of Cytology, 417 VA (NIMTS) Hospital, Athens, Greece

Corresponding author: Evangelos Tsiambas, MD, MSc, PhD.
Email: tsiambasecyto@yahoo.gr

The impact of time to surgery in different tumor subtypes in breast cancer patients who received neoadjuvant chemotherapy

Dear Editor,

The optimal timing from neoadjuvant chemotherapy (NAC) to surgery in patients with breast cancer has not been well-known. Lai and colleagues investigated whether time to surgery affects patient outcomes in breast cancer patients who received NAC. They concluded that there were no statistically significant differences in pCR, DFS, OS, surgical complications, and rates of conversion from mastectomy to BCS, among breast cancer patients receiving surgery <4 weeks, 4-8 weeks, or >8 weeks after the last dose of NAC [1]. However, the authors did not evaluate the impact of time to surgery in different tumor subtypes (hormone receptor positive [(HR-positive)/HER2-negative, HER2-positive, or triple negative breast cancer (TNBC)]. TNBC accounts for 15% of breast carcinomas and, when present as early-stage disease, they are associated with higher rates of recurrence and early distant metastasis risk when compared to hormone receptor positive and HER-2 positive breast cancers [2]. Two recent studies reported that a delay in initiating adjuvant chemotherapy was associated with adverse outcomes in TNBC [3,4]. Furthermore, Morante and colleagues in their retrospective study evaluated the influence of the time to start adjuvant chemotherapy (TTC) in the outcomes of 687 TNBC patients. They concluded that a delay in TTC ≥ 30 days was associated with poorer outcomes [5]. Therefore, tumors with high proliferative index like TNBC or HER2-positive preferably might get surgery within 4 weeks after completion of chemotherapy. This issue merits further investigation.

References

1. Budakoglu B, Altundag K, Aksoy S et al. Outcome of 561 non-metastatic triple negative breast cancer patients: multi-center experience from Turkey. *J BUON* 2014;19:872-8.
2. Lai V, Hajjaj O, Le D, Shokoohi A, Chia S, Simmons C. Impact of wait time from neoadjuvant chemotherapy to surgery in breast cancer: Does time to surgery affect patient outcomes?: Time from Neoadjuvant Chemotherapy to Surgery. *Breast Cancer Res Treat*. 2020 Oct 1. doi: 10.1007/s10549-020-05894-x. Epub ahead of print. PMID: 33001336.
3. De Melo Gagliato D, Gonzalez-Angulo AM, Lei X et al. Clinical impact of delaying initiation of adjuvant chemotherapy in patients with breast cancer. *J Clin Oncol* 2014;32:735-44.
4. Chavez-MacGregor M, Clarke CA, Lichtensztajn DY, Giordano SH. Delayed initiation of adjuvant chemotherapy among patients with breast cancer. *JAMA Oncol* 2016;2:322-9.
5. Morante Z, Ruiz R, Araujo JM et al. Impact of the delayed initiation of adjuvant chemotherapy in the outcome of triple-negative breast cancer, *Clin Breast Cancer* 2020, doi: <https://doi.org/10.1016/j.clbc.2020.09.008>.

Kadri Altundag

MKA Breast Cancer Clinic, Ankara, Turkey.

Corresponding author: Kadri Altundag, MD.
Email: altundag66@yahoo.com

Association between nanobacteria and microcalcifications in breast

Dear Editor,

Nanobacteria have recently been described as novel microorganisms characterized by small size, slow growth, and the ability to form calcium phosphate crystals at neutral

pH and at physiologic calcium and phosphate concentrations. They are gram-negative, have a unique structure and apparent nucleic acid, and their growth *in vitro* is best inhibited by tetracycline. Nanobacteria have been discovered in human and cow blood and commercial cell culture sera,

and have been hypothesized to mediate tissue calcifications [1]. Haghayeghi et al [2] reviewed radiopathologic findings of breast biopsies and excisions to re-examine the clinicopathologic significance of calcium oxalate (CaOx) deposits and to ascertain potential radiologic characteristics for their identification. As authors stated the etiology and mechanism of mammary CaOx deposition remain poorly understood. Data in the literature suggest that deposition of the bone-specific mineral hydroxyapatite results from an active biological process [3]. Since nanobacteria have been shown to contribute to different benign and malignant calcifications, nanobacteria may also contribute to microcalcifications in breast cancer [1]. This proposal needs to be investigated by microbiological analysis of microcalcified breast tissue.

References

1. Altundag K, Altundag O, Akyurek S, Atik MA. Possible association between nanobacteria and malig-

nant microcalcifications in breast cancer. *Breast J* 2006;12:287.

2. Haghayeghi K, Najibi M, Wang H, Donegan L, Wang Y. Clinicopathologic update of calcium oxalate in breast: A 15-year retrospective review [published online ahead of print, 2020 Jun 21]. *Breast J* 2020; 26:1736-41.
3. Safioleas PM, Koulocheri D, Michalopoulos N et al. The value of stereotactic vacuum assisted breast biopsy in the investigation of microcalcifications. A six-year experience with 853 patients. *J BUON* 2017;22:340-6.

Kadri Altundag

MKA Breast Cancer Clinic, Ankara, Turkey.

*Corresponding author: Kadri Altundag, MD.
Email: altundag66@yahoo.com*

Do molecular subtypes affect overall survival after radiation therapy for breast cancer patients with brain metastases?

Dear Editor,

Breast cancer is a heterogeneous disease divided into subtypes based on molecular features such as hormonal receptors (HR) and human epidermal growth factor receptor 2 (HER2) status. Approximately 10-16% of patients with metastatic breast cancer show brain metastases (BMs) during the course of their disease. One retrospective study investigated clinical differences among biological subtypes in 315 breast cancer patients with BMs after targeted therapy introduction. Overall survival (OS) from the start of treatment of BM (OSBM) was 20 months for HER2-/HR+; 22 months for HER2+/HR+; 24 months for HER2+/HR-; and 9 months for triple negative ($p < 0.001$). Triple negative disease showed lower OSBM compared with other subtypes, with a hazard ratio of 1.9 ($p < 0.001$) [1]. Furthermore, Fan and colleagues [2] investigated whether systemic therapy (ST) use surrounding radiation therapy (RT) predicts OS after RT for patients with BMs. The cancer diagnoses were: lung ($n=1692$, 55%), breast ($n=544$, 18%), gastrointestinal ($n=245$, 8%), melanoma ($n=243$, 8%), kidney ($n=104$, 3%), and other ($n=267$, 9%). In comparison to the 2096 non-recipients of ST after RT, the median OS of the 999 recipients of ST after RT was 5.0 months longer ($p < 0.0001$). They concluded that the type and timing of ST use surrounding

RT predict OS for patients with BMs. However, the authors did not look at the association between molecular subtypes and OS after RT for breast cancer patients with BMs. It would be expected that molecular subtypes of breast cancer patients with BMs in particular might affect OS after RT besides ST. This issue merits further investigation.

References

1. Bastos DCA, Maldaun MVC, Sawaya R et al. Biological subtypes and survival outcomes in breast cancer patients with brain metastases in the targeted therapy era. *Neurooncol Pract* 2018;5:161-9.
2. Fan KY, Lalani N, LeVasseur N et al. Type and timing of systemic therapy use predicts overall survival for patients with brain metastases treated with radiation therapy. *J Neurooncol* 2020 Nov 18. doi: 10.1007/s11060-020-03657-8.

Kadri Altundag

MKA Breast Cancer Clinic, Ankara, Turkey.

*Corresponding author: Kadri Altundag, MD.
Email: altundag66@yahoo.com*

Viral infections in meningiomas

Dear Editor,

The histological substrate of meningiomas is the arachnoid cap cells of the meninges on the periphery of the

brain. Brain tissue invasion is the most critical histopathological evidence of aggressive biological behavior of the tumor. Furthermore, the extracranial metastatic potential of meningiomas is low, and their metastatic activity and pen-

etration is extremely rare in significant series of meningiomas which detected gross chromosomal and specific gene aberrations (rearrangements/intra- or inter- translocations, gains, frame-shift deletions/insertions, point-driver mutations or in-frame fusions) which also reflect their grades of differentiation (Grade I-III) [1]. Interestingly, meningiomas are the second most common brain tumours and the most common intracranial primary central nervous system (CNS) tumours in adults. Recurrence of these tumours - especially in higher grade meningiomas - is correlated with an aggressive biological behaviour affecting the response rates to surgery/radiation applied therapeutic regimens. Especially, in the cases of recurrent meningiomas with atypical/anaplastic histotypes addition of radiation in the corresponding chemotherapeutic regimens should be an advantage for subgroups of patients [2].

Besides the genetic and epigenetic changes that lead to neoplastic and malignant transformation of the normal meningeal cells, there are limited data regarding viruses' involvement in this process or their presence as a complication in neurosurgical procedures. Some studies reported a rare implication of Herpes Simplex Virus type 2 (HSV-2) in postsurgical meningioma elective resection [3]. Similarly, HSV-1 mediated encephalitis is also exceedingly rare, whereas both need immediate appropriate antiviral therapy. Concerning persistent viral infection -as a significant etiopathogenetic factor in aggressive brain malignancies such as glioblastoma and also meningiomas development and progression- there are controversial and poor results. A next generation sequencing (NGS)-based virome assessment analysis regarding predominantly human cytomegalovirus (HCMV), Epstein-Barr (EBV), HSV 6/7, Human PapillomaVirus (HPV) and Hepatitis B Virus (HBV) reported a potential low percentage association between only HPV and / or HBV in glioblastoma multiforme (GBM) and meningioma development [4]. Additionally, another study group analyzed the previously referred set of viruses by implementing a combined polymerase chain reaction (PCR), immunohis-

tochemistry (IHC), and serological analyses mediated by enzyme-linked immunosorbent assay (ELISA) protocol. They failed to detect important levels of these viruses in the examined brain tumors [5].

References

1. Yuzawa S, Nishihara H, Tanaka S. Genetic landscape of meningioma. *Brain Tumor Pathol* 2016;35:237-47.
2. Chohan MO, Ryan CT, Singh R et al. Predictors of treatment response and survival outcomes in meningioma recurrence with atypical or anaplastic histology. *Neurosurgery* 2018;82:824-32.
3. Berger A, Shahar T, Margalit N. Herpes Simplex Type 2 Encephalitis After Craniotomy: Case Report and Literature Review. *World Neurosurg* 2016; 88:691.e9-12.
4. Strong MJ, Blanchard E, Lin Z et al. A comprehensive next generation sequencing-based virome assessment in brain tissue suggests no major virus - tumor association. *Acta Neuropathol Commun* 2016;4:71-5.
5. Poltermann S, Schlehofer B, Steindorf K, Schnitzler P, Geletneky K, Schlehofer JR. Lack of association of herpesviruses with brain tumors. *J Neurovirol* 2006;12:90-9.

Maria Adamopoulou¹, Dimitrios Roukas², Stylianos Mastrotrionikolis³, Evangelos Tsiambas⁴

¹Department of Biomedical Sciences, University of West Attica, Athens, Greece; ²Department of Psychiatry, 417 Veterans Army Hospital (NIMTS), Athens, Greece; ³Medical School, University of Heraklion, Crete, Greece; ⁴Department of Cytology, 417 Veterans Army Hospital (NIMTS), Athens, Greece.

Corresponding author: Evangelos Tsiambas, MD, MSc, PhD. Email: tsiambasecyto@yahoo.gr

Is up-front surgery associated with fatality of disease in breast cancer patients with *de novo* metastases?

Dear Editor,

The incidence of *de novo* metastases (mets) in breast cancer (BC) patients with a new diagnosis is up to 10%. Surgical excision of the primary tumour is reserved in patients with significant symptoms from the primary tumour. Survival benefit of surgical removal of the primary tumour remains controversial [1]. Sakhuja and their colleagues [2] investigated patterns of *de novo* mets and association with BC-specific mortality across subtypes and racial groups. A total of 204,941 BC patients were included in this analysis. The authors concluded that site and fatality of *de novo* mets vary by subtype and by race. In their cohorts, first-course treatment was surgery in 40.2-49.4% of all molecular subtypes. As expected, initial surgery was more common in HR+/HER2 negative cases. However, the authors did not mention the role of surgery in regard to fatality of disease. A randomized trial comparing resection of primary tumor with no surgery by Soran et al [3] was

reported recently. In this Turkish study, however, stage IV patients were offered upfront surgery. Furthermore, patients in locoregional treatment (LRT) group had more HR+ BC and less triple negative BC. The final analysis showed significant 10-year OS benefit with LRT (46 months) vs 35 months (HR=0.71). Based on the multivariate analysis, LRT was the only prognostic factor that was associated with better OS (p=0.03). The authors concluded that in *de novo* stage IV BC setting, those patients who underwent upfront surgery followed by systemic therapy had a 58% higher chance to live at 5 years compared with those who received systemic therapy only. It may be argued that selection bias may be reasonable in that the patients selected for surgery may already have better prognosis at diagnosis of metastatic BC due to low metastatic disease burden or indolent tumor biology like more cases with HR+ BC cases. In conclusion, decision for starting with upfront surgery in *de novo* metastases need multidisciplinary discussion for each case.

References

1. Xue F, Yu L, Lin Y et al. Surgery in initially metastatic breast cancer: prognosis is associated with patient characteristics and timing of surgery. *JBUON* 2019;24:543-8.
2. Sakhuja S, Deveaux A, Wilson LE et al. Patterns of de-novo metastasis and breast cancer-specific mortality by race and molecular subtype in the SEER population-based dataset. *Breast Cancer Res Treat* 2020 Nov 11. doi: 10.1007/s10549-020-06007-4.
3. Soran A, Ozmen V, Ozbas S et al. Randomized trial comparing resection of primary tumor with no surgery in stage IV breast cancer at presentation: protocol MF07-01. *Ann Surg Oncol* 2018;25:3141-9.

Kadri Altundag

MKA Breast Cancer Clinic, Ankara, Turkey.

Corresponding author: Kadri Altundag, MD.

Email: altundag66@yahoo.com

Do all triple-negative breast cancer patients have to receive adjuvant chemotherapy within 30 days after surgery; do subtypes matter?

Dear Editor,

Triple-negative breast cancer (TNBC) accounts for 15% of breast carcinomas and when present as early-stage disease, it is associated with higher rates of recurrence and early distant metastasis risk when compared to hormone receptor positive and human epidermal growth factor receptor (HER-2) positive breast cancers [1]. TNBC is a heterogeneous disease. It is a well-known fact that all TNBC cases do not show the same pathology and same prognostic factors. For example, medullary carcinoma or adenocystic carcinoma cases with TNBC show better overall survival compared to metaplastic cases with TNBC features [2]. Morante and colleagues in their retrospective study evaluated the influence of the Time To start adjuvant Chemotherapy (TTC) in the outcomes of 687 TNBC patients and concluded that a delaying in $TTC \geq 30$ days was associated with poorer outcomes. Their data suggest that several efforts should be conducted to avoid a delayed TTC in TNBC patients [3]. The authors did not evaluate TNBC histological subtypes. Therefore, for those TNBC patients with better prognostic features,

a delaying TTC might not be associated with poorer survival. This issue merits further investigation.

References

1. Budakoglu B, Altundag K, Aksoy S et al. Outcome of 561 non-metastatic triple negative breast cancer patients: multi-center experience from Turkey. *JBUON* 2014;19:872-8.
2. Altundag K. Have all triple-negative breast cancer patients worse breast cancer-specific survival? *Breast* 2017;36:102.
3. Morante Z, Ruiz R, Araujo JM et al. Impact of the delayed initiation of adjuvant chemotherapy in the outcome of triple-negative breast cancer, *Clin Breast Cancer* (2020), doi: <https://doi.org/10.1016/j.clbc.2020.09.008>.

Kadri Altundag

MKA Breast Cancer Clinic, Ankara, Turkey.

Corresponding author: Kadri Altundag, MD.

Email: altundag66@yahoo.com