

## SHORT COMMUNICATION

**ER–/PR+ SUBSET OF INVASIVE BREAST CARCINOMA (IBC):  
A DISTINCT PHENOTYPE WITH GOOD PROGNOSIS**SIMONA STOLNICU<sup>1</sup>, ORSOLYA BAUER<sup>2</sup>, ADRIAN NAZNEAN<sup>3</sup>, CRISTIAN PODOLEANU<sup>4</sup>, RAREȘ GEORGESCU<sup>2</sup><sup>1</sup>Department of Pathology, The University of Medicine and Pharmacy of Tîrgu Mureș, Tîrgu Mureș, Romania<sup>2</sup>Department of Surgery, The University of Medicine and Pharmacy of Tîrgu Mureș, Tîrgu Mureș, Romania<sup>3</sup>Department of Foreign Languages, The University of Medicine and Pharmacy of Tîrgu Mureș, Tîrgu Mureș, Romania<sup>4</sup>Department of Cardiology, The University of Medicine and Pharmacy of Tîrgu Mureș, Tîrgu Mureș, Romania

The expression of the estrogen (ER) and progesterone (PR) receptors in IBC patients represents a well-known prognostic and predictive factor. The existence of ER–/PR+ as a distinct phenotype, however, is controversial as well as is its prognostic significance. The aim of the study was to assess the incidence and prognosis in patients with ER–/PR+ IBC.

One hundred and twelve patients with IBC were analyzed regarding ER/PR profile and survival. GraphPad prism 6 for Windows and Kaplan Mayer curve were used to determine overall survival (OS) and disease-free survival (DFS), with  $p < 0.05$  as statistically significant.

Of the 112 IBC patients, 75% were ER+/PR–, 16.07% were ER–/PR–, 7.14% were ER+/PR+ and only 1.78% were ER–/PR+. OS was 100% in the ER–/PR+ group and 91.6% in the ER+/PR+ group. The lowest OS was found in the ER–/PR– group (72.2%), while OS was 100% in ER–/PR+ group. Regarding DFS, there were no statistically significant differences in the four groups ( $p = 0.11$ ), although the highest DFS was found in the ER–/PR+ group (100%). ER–/PR+ tumors were associated with younger age ( $p = 0.72$ ), smaller tumor diameter ( $p = 0.27$ ), absence of lymph node metastases, and HER2 overexpression.

Our results suggest that ER–/PR+ cases represent the rarest phenotype in IBC cases but its association with the best OS and DFS in other ER/PR phenotypes indicates an independent predictive value of PR for treatment considerations.

**Key words:** breast pathology, breast cancer, immunohistochemistry, hormone receptors, management.

**Introduction**

Breast cancer is the most frequently encountered malignant tumour in females worldwide. The expression of oestrogen (ER) and progesterone (PR) receptors in invasive breast carcinoma (IBC) patients represents a well-known prognostic and predictive parameter. Most IBCs are ER+/PR+ or ER+/PR–

while a small subset of them are ER–/PR–. The existence of IBCs with an ER–/PR+ as a distinct phenotype however, is controversial as well as its prognostic significance.

Most papers published on this topic emphasise that the ER–/PR+ subset of IBCs does not really exist and that the independent predictive value of PR+ for treatment considerations is also in question [1, 2].

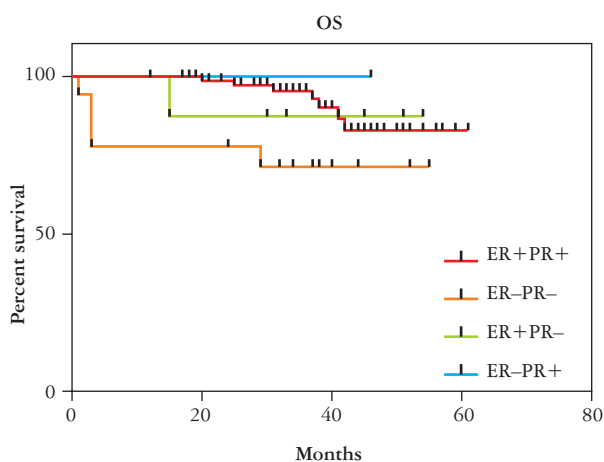


Fig. 1. Overall survival (OS) Kaplan Mayer rates comparison in ER+/PR+, ER-/PR-, ER+/PR- and ER-/PR+ cases

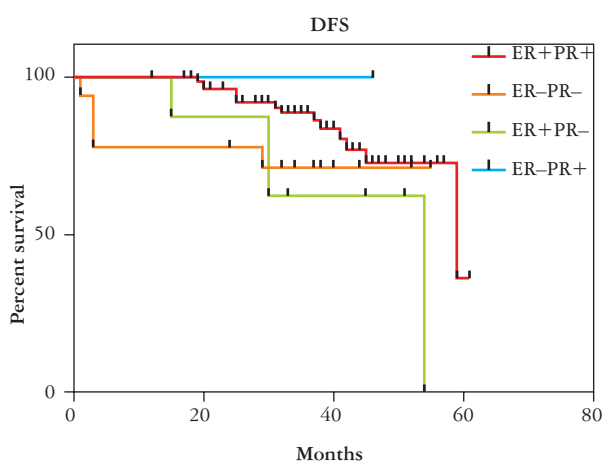


Fig. 2. Disease-free survival Kaplan Mayer rates comparison in ER+/PR+, ER-/PR-, ER+/PR- and ER-/PR+ cases

Also, most authors believe that the ER status is the only most important predictive parameter in IBC. Some other authors have demonstrated that IBCs being ER-/PR+ develop with a frequency up to 4% of all cases and this subset of tumours is associated with an improved 10-year survival for stage I compared with ER+/PR+ cases, lacking, however, any significance when including all cases [3]. In contrast, other authors have demonstrated that ER-/PR+ IBCs which occur in younger patients are characterised by a higher microscopic grade and show HER2+ overexpression more frequently although the OS (overall survival) and RFS (relapse-free survival) are similar to the ER+/PR+ cases and better than in the ER-/PR- cases [4, 5]. Moreover, one study demonstrated that ER-/PR+ cases receiving endocrine therapy had a higher response to endocrine therapy when compared with ER+/PR-

tumours and thus it is important to identify them in the routine practice with the help of ancillary studies such as immunohistochemistry as well as RNA-base assessment [6].

We read with great interest the recent paper on clinico-pathological characteristics on ER-/PR+ breast cancers written by Ahmed *et al.* [7]. In that paper, the authors investigated an initial cohort of 267 ER-/PR+ cases by reviewing tissue microarrays and repeated immunohistochemistry for ER and PR markers and subsequently found only 92 tumours being confirmed to have an ER-/PR+ profile, this phenotype accounting for 1.1% of all IBCs in that study. Moreover, the ER-/PR+ tumours showed distinct clinico-pathological features, a trend for early recurrence and poorer overall survival (OS) compared with patients with ER+/PR+ and similar to ER-/PR- tumours [7].

## Report and discussion

Because in our routine practice we have encountered ER-/PR+ IBC cases, in the present study our aim was to assess the incidence and prognosis in patients with this particular phenotype. For this purpose, 112 patients with IBC were retrospectively analysed regarding the ER/PR profile and survival. These patients were diagnosed on core biopsy and surgically treated before the oncological treatment was administered. The ER and PR markers were reanalysed on full slides obtained from the surgical specimen using Estrogen Receptor Clone 6F11, dilution 1 : 100, Novocastra, Newcastle, UK and Progesterone Receptor, Clone 312, dilution 1 : 100, Novocastra, Newcastle, UK. Both markers were considered as positive if at least 1% positive tumour nuclei were present within the tumour (with positive internal and/or external control), according to international guidelines [8]. All cases were reviewed by an experienced breast pathologist (SS). GraphPad prism 6 for Windows and Kaplan Mayer curve were used to determine overall survival (OS) and disease-free survival (DFS), with  $p < 0.05$  as statistically significant.

Of the 112 IBC patients, 75% were ER+/PR+, 16.07% were ER-/PR-, 7.14% were ER+/PR- and only 1.78% were ER-/PR+. Overall survival was 100% in ER-/PR+ group and 91.6% in the ER+/PR+ group. The lowest OS was found in the ER-/PR- group (72.2%) (Fig. 1). Regarding the DFS, there were no statistically significant differences between the four groups ( $p = 0.11$ ), although the highest DFS was found in the ER-/PR+ group (100%) followed by the ER+/PR+ group (83.3%), where local recurrences were found in 5.95% of cases, 9.52% of which had distant metastases (Fig. 2). The lowest DFS rate was found in the ER+/PR- cases (50%). Compared with ER+ tumours, ER-/PgR+

tumours were associated with younger age ( $p = 0.72$ ) and smaller tumour diameter ( $p = 0.27$ ), although this was not statistically significant. Also, in our group, none of the ER-/PR+ tumours presented lymph node metastases or HER2 overexpression/amplification.

Similar to the paper by Ahmed *et al.* [7], our results suggest that ER-/PR+ cases represent the rarest phenotype among IBC cases, but in our group, its association with the best OS and DFS among other ER/PR phenotypes indicates an independent predictive value of PR for treatment considerations.

In conclusion, ER-/PR+ IBCs cases do exist although they are rare, they are characterised by distinct clinical and molecular features and immunohistochemical studies as well as RNA-base assessment may help to identify them in order to receive the best treatment based on both adjuvant endocrine and chemotherapy.

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*The authors declare no conflict of interest.*

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