

# TREATMENT ALGORITHM AND DIRECT COSTS IN TREATMENT OF HR+/HER2- POST MENOPAUSAL ADVANCED/METASTATIC BREAST CANCER PATIENTS IN TURKEY

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## OBJECTIVES

The objectives of this study were to understand the treatment algorithm of HR+/HER2- post menopausal advanced/metastatic breast cancer in Turkey and to calculate the direct treatment cost of the disease based on this algorithm.

## METHODS

Delphi panel method was used. In this regard, a questionnaire form about the epidemiology, diagnosis, treatment, monitoring, palliative care and adverse events of HR+/HER2- postmenopausal advanced/metastatic breast cancer were prepared in order to identify the number of patients, type and frequency of healthcare resources used. The form was filled in by five experts from public and private tertiary care institutions based on their daily practice. Then the answers were aggregated and a consensus form indicating the treatment algorithm was formed. The resources were priced by using the official price lists of the Social Security Institution and the Ministry of Health.

## RESULTS

The study results revealed the epidemiologic outlook and medical resources used in diagnosis, 1<sup>st</sup>/2<sup>nd</sup>/3<sup>rd</sup> and 4<sup>th</sup> lines of treatment, monitoring, palliative care and adverse events.

Within this scope, the ratio of the HR+/HER2- post menopausal metastatic breast cancer patients is found to be 4.6% among whole breast cancer patients (Table 1).

**Table 1:** Epidemiologic outlook of breast cancer according to panel results

Ratio of women (over 15 years old) diagnosed with breast cancer in Turkey	38.30 /100,000
Ratio of metastatic (Stage 4) breast cancer patients among whole breast cancer patients	27.00 %
Ratio of metastatic breast cancer patients progressed from early stage among whole breast cancer patients	16.70 %
Ratio of patients developing metastasis in first 12 months	33.60 %
Ratio of patients developing metastasis after first 12 months	66.40 %
Ratio of breast cancer patients with metastasis at the time of diagnosis among the whole breast cancer patients	9.90 %
Ratio of breast cancer patients among age groups	
15-34	13.40 %
35-54	39.20 %
55-64	29.80 %
65 and over	17.60 %
Ratio of pre-menopausal and post-menopausal patients among whole breast cancer patients	
Pre-menopausal	43.00 %
Post-menopausal	57.00 %
Ratio of HR+, HER2- breast cancer patients among post-menopausal breast cancer patients	73.50 %

In order to determine treatment algorithm for HR+/HER2- post menopausal advanced/metastatic breast cancer patients, distribution of patients among treatment lines, rate of transmission to next line treatments are investigated (Table 2). Distribution and transmission rates have been derived from answers of panel participants. Panel participants gave a snapshot of their current patients' distribution among therapy lines and proportion of patients receiving further line of treatment.

**Table 2:** Distribution of HR+/HER2- post menopausal metastatic breast cancer patients among 1<sup>st</sup> / 2<sup>nd</sup> / 3<sup>rd</sup> and 4<sup>th</sup> line treatments and rate of transmission to next line treatments in 1 year

	1 <sup>st</sup> line treatment	2 <sup>nd</sup> line treatment	3 <sup>rd</sup> line treatment	4 <sup>th</sup> line treatment
Ratio of HR+ /HER2- metastatic breast cancer patients receiving 1 <sup>st</sup> / 2 <sup>nd</sup> / 3 <sup>rd</sup> or 4 <sup>th</sup> line treatment among whole breast cancer patients treated in one year	50%	25%	17%	8%
Rate of transmission	from 1 <sup>st</sup> to 2 <sup>nd</sup> line treatment	from 2 <sup>nd</sup> to 3 <sup>rd</sup> line treatment	from 3 <sup>rd</sup> to 4 <sup>th</sup> line treatment	
	32%	56%	62%	

For each treatment line percentage of utilization of hormonal therapies, targeted therapies, chemotherapy, chemotherapy combinations, radiotherapy and surgery are determined (Table 3). While drug therapies are received by all patients, some of them receive radiotherapy and surgery additionally.

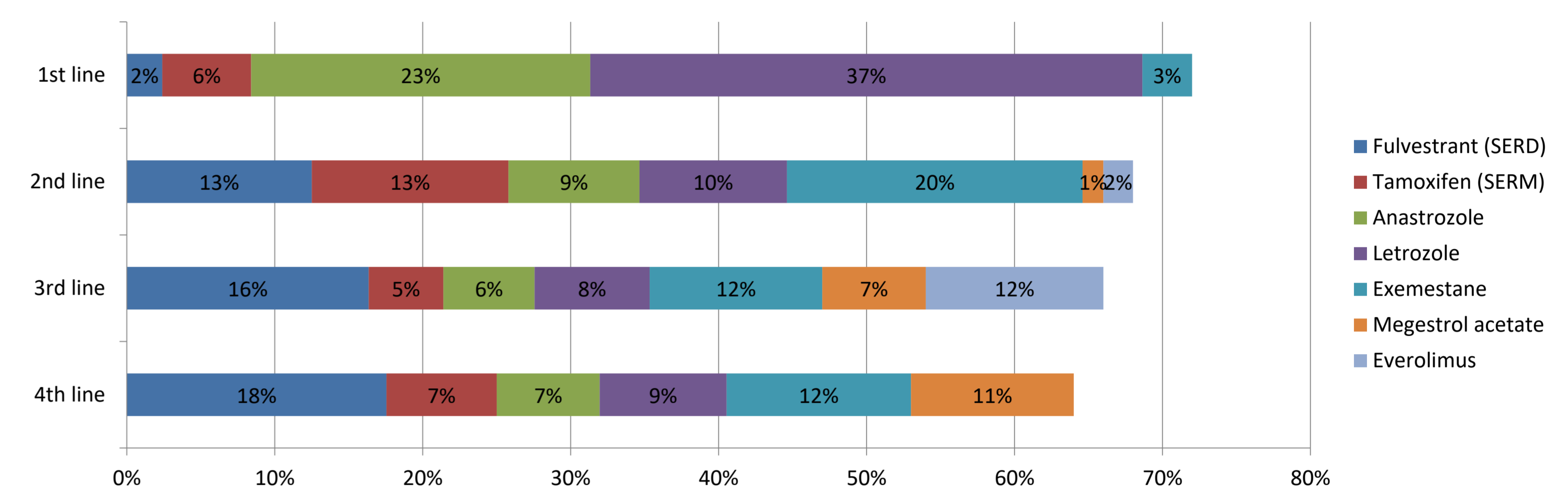
Drug therapies are further broken down by agents for each line, revealing an increase in chemotherapy and chemotherapy combinations by further lines (Figure 1a,1b).

## RESULTS

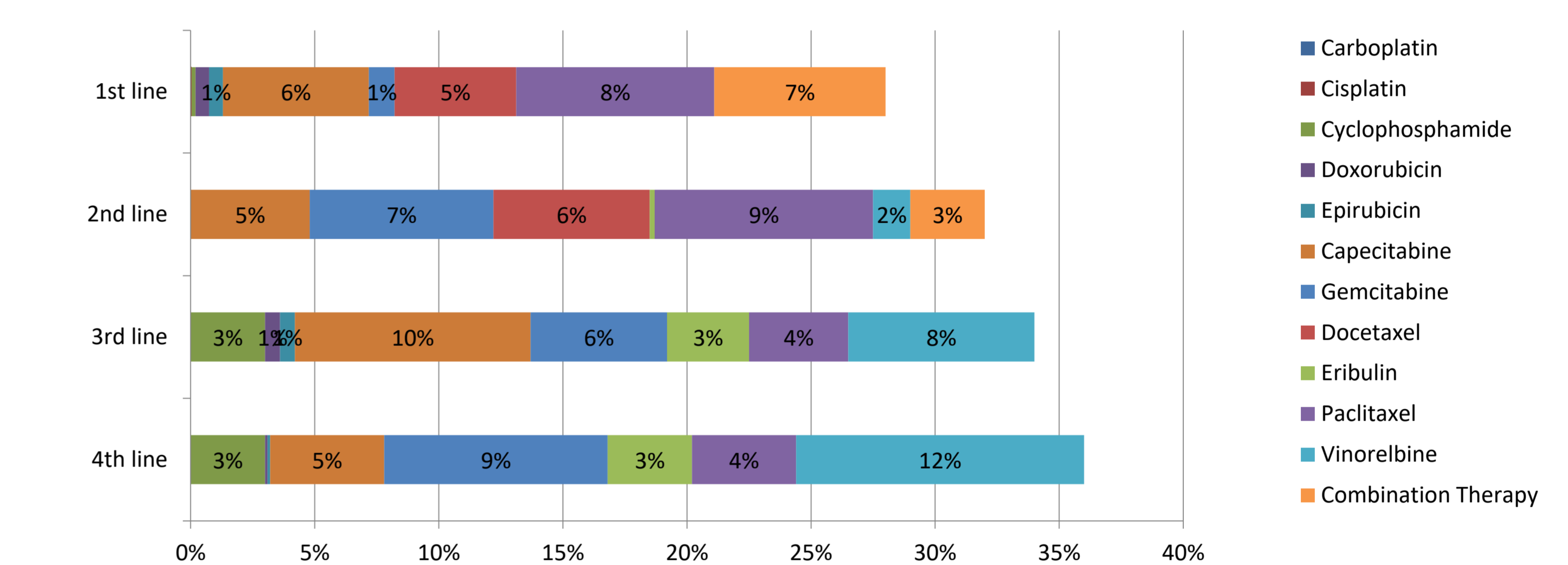
**Table 3:** Therapy utilization in HR+/HER2- post menopausal metastatic breast cancer patients

	1st line	2nd line	3rd line	4th line
Hormonal Therapy	72%	66%	54%	64%
Targeted Therapy	0%	2%	12%	0%
Chemotherapy	21%	29%	34%	36%
Chemotherapy Combinations	7%	3%	0%	0%
Radiotherapy	33%	29%	33%	29%
Surgery	10%	4%	2%	2%

**Figure 1a:** Percentage of HR+/HER2- post menopausal metastatic breast cancer patients receiving hormonal therapy and targeted therapy per treatment line by agents



**Figure 1b:** Percentage of HR+/HER2- post menopausal metastatic breast cancer patients receiving chemotherapy either as monotherapy or combination therapy per treatment line by agents



Agents with less than 1% utilization in a given line have not been labeled in the figure. Combination therapies are Doxorubicin+Cyclophosphamide, Cyclophosphamide+Doxorubicin+Fluorouracil, Doxorubicin+Taxol, Taxol+Carboplatine, Docetaxel-Capecitabine, Gemcitabine+Carboplatin, Vinorelbine+Gemcitabine, Capecitabine+Docetaxel, Gemcitabine+Paclitaxel, Gemcitabine+Cisplatin

Costs according to health care resource utilization are demonstrated in Table 4. These cost items are calculated annually and do not reflect cumulative cost per patient along whole treatment process.

**Table 4:** Average direct costs of HR+/HER2- post menopausal metastatic breast cancer by cost items

	Average cost per patient (\$*)
Diagnosis	265.95
Treatment	
1 <sup>st</sup> line	1285.71
2 <sup>nd</sup> line	1591.89
3 <sup>rd</sup> line	4359.55
4 <sup>th</sup> line	1973.48
Monitoring	
1 <sup>st</sup> line	901.31
2 <sup>nd</sup> line	1036.37
3 <sup>rd</sup> line	949.24
4 <sup>th</sup> line	1018.07
Adverse events	111.25
Palliative care	412.57

\* \$ = 2.72 TL (Average Exchange rate in 2015)

## CONCLUSIONS

The study revealed the treatment approaches of participants for HR+/HER2- post menopausal advanced/metastatic breast cancer patients to represent mostly tertiary care hospital practice. Costs to public payer have been calculated, taking into account all direct medical costs including adverse events, revealing differences between treatment lines.

As a limitation of the study it should be noted that the five participants in the panel are from tertiary care centers. The treatment patterns may differ in different centers and across the country. Panelists estimate chemotherapy usage in early lines of treatment is higher country wide than their practice, considering institutions other than tertiary care.

Treatment patterns show that share of chemotherapy increases in subsequent lines. This points to potential benefits of novel therapies with high progression free survivals at first line, which would delay subsequent use of chemotherapy.<sup>1</sup>

In addition, this study include on ly direct costs, indirect costs were not taken into consideration within the study scope. Therefore, further studies including indirect costs may allow more comprehensive understanding of disease burden.