

A Budget-Impact Analysis of Adjuvant Pertuzumab and Trastuzumab in Early HER2-Positive Breast Cancer

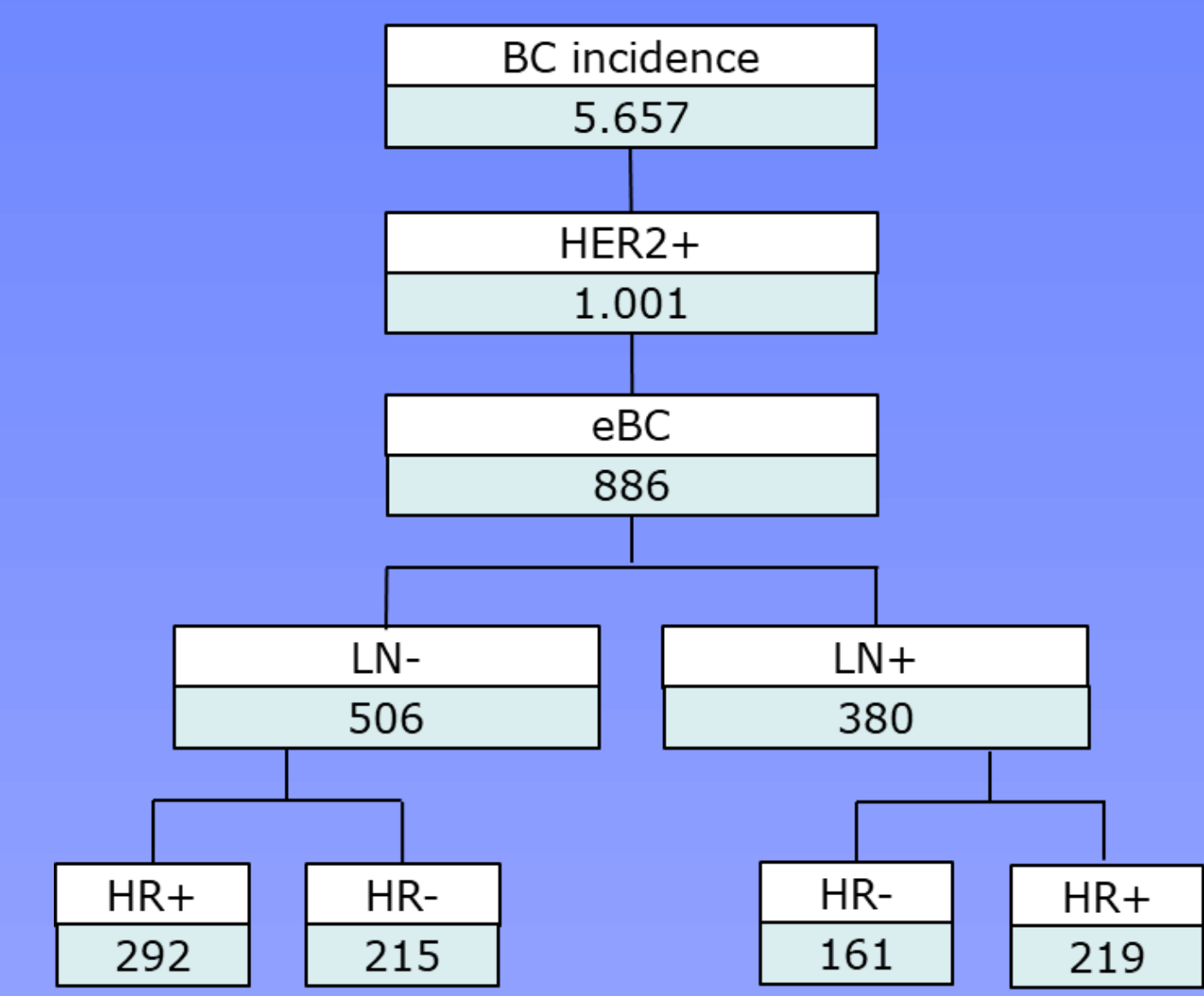
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Objectives

Breast Cancer is the most common cancer in women. In 2015 5480 new cases were noted in Austria; 90.5% with operable early breast cancer (eBC) and among these approximately 18% with HER2 over-expression. This expression is associated with a more aggressive disease, higher recurrence rate, and increased mortality. Trastuzumab is a monoclonal antibody targeting the HER2 receptor and has become the standard of care (SOC) in addition to chemotherapy for the treatment of HER2+ Breast Cancer. The APHINITY trial has demonstrated that adding the second HER2-targeted antibody Pertuzumab in the early setting (eBC) improved outcomes compared to SOC.

Fig. 1: Patient-Flow of HER2+ patients extrapolated to 2018

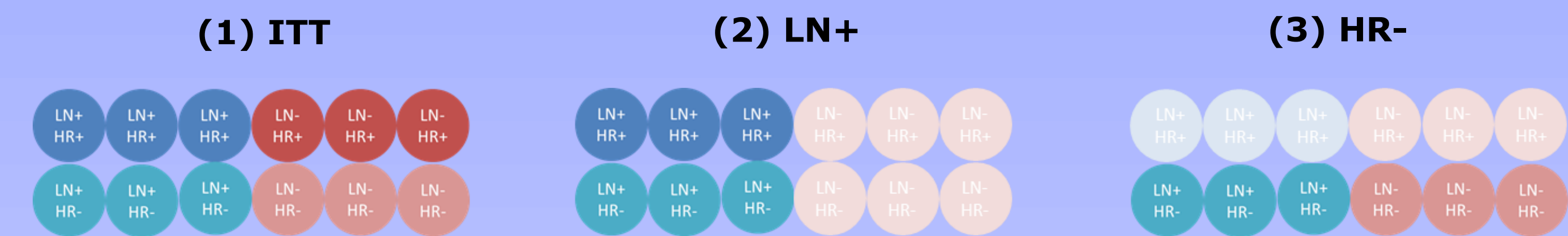


Source: own developed

The aim of the Budget-Impact model (BIM) is to determine the immediate budgetary impact (in a 5-year frame) of the neo- and adjuvant use of Pertuzumab + Trastuzumab and chemotherapy (APHINITY scheme) compared to a regime without adjuvant Pertuzumab in either all eligible HER2+ patients (ITT) or only in the predefined high-risk groups (node positive (LN+), 42.9% of HER2+ patients / hormone receptor negative (HR-), 57.6% of HER2+ patients).

The BIM is performed on the basis of the following subgroups of newly diagnosed HER2+ breast cancer patients:

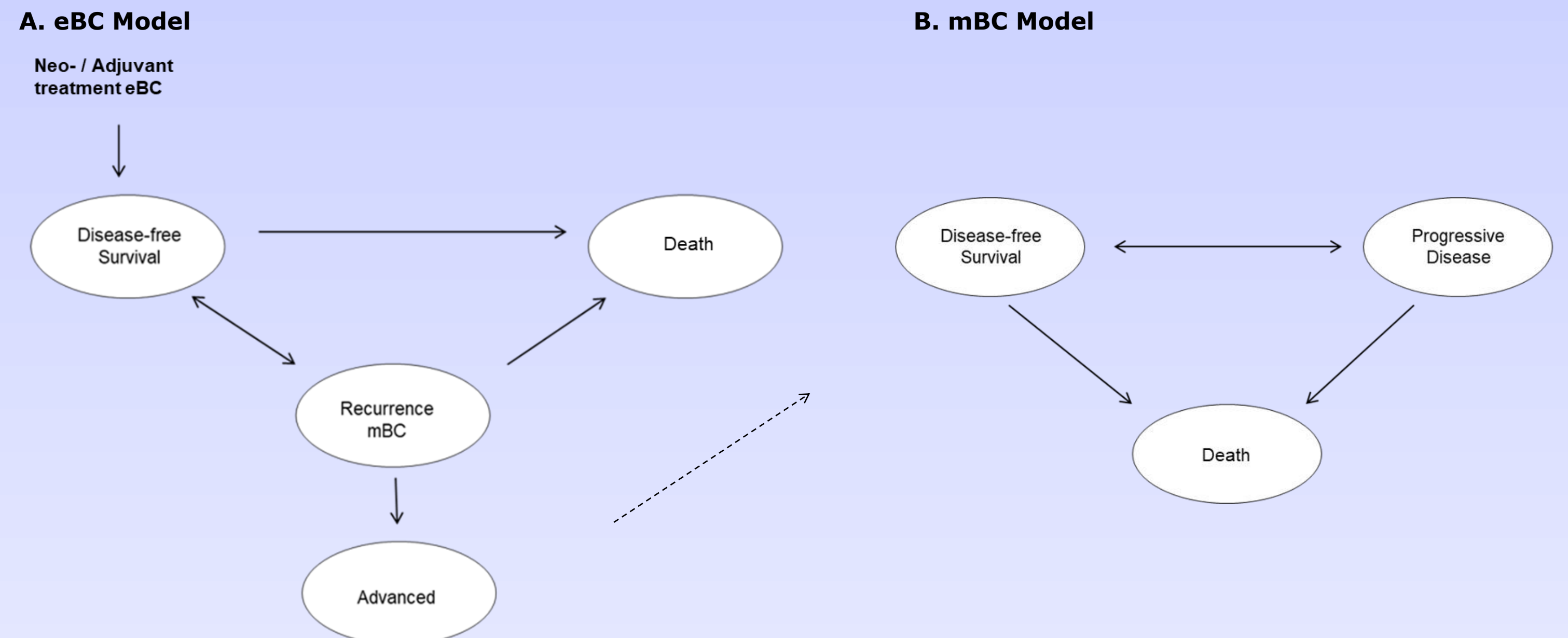
- (1) ITT population of the APHINITY trial (estimation for 2018: n = 886)
- (2) LN+ population (estimation for 2018: n= 380)
- (3) HR- population (estimation for 2018: n= 376)



Methods

A multi-cohort, HER2+ population-based model was developed over a 5-year time-horizon, which includes two model parts (eBC and mBC) with the following states: (a) eBC (disease free survival, recurrence and death) and (b) mBC (disease-free-survival, progressive disease and death). Results show the Budget-Impact over 5 years (including drug costs, monitoring costs, adverse event costs, costs of recurrence (mBC) and end of life costs, but not considering socioeconomic costs such as avoided inability to work etc) for the different risk-groups from the payer's perspective.

Fig. 2: Model Design



Source: own developed

Model comparators

Model eBC (SOC ± adjuvant Pertuzumab)

- SOC + adjuvant Pertuzumab:**
- neoadjuvant (3-6 cycles): Pertuzumab + Trastuzumab and chemotherapy
 - adjuvant completion to one year with Pertuzumab + Trastuzumab and chemotherapy
- SOC:**
- neoadjuvant (3-6 cycles): Pertuzumab + Trastuzumab and chemotherapy
 - adjuvant completion to one year with Trastuzumab and chemotherapy

B: Modell mBC (both arms)

- 1st Line: Pertuzumab + Trastuzumab and chemotherapy
- 2nd Line : Trastuzumab Emtansin
- 3rd Line: Trastuzumab and chemotherapy

Resource Use and Costs

The BIM includes drug costs, staff and material costs, monitoring costs, adverse event costs, costs of recurrence (mBC) and end of life costs over the 5 year time horizon. Data on the use of resources was collected in two steps. First, the medical resources were derived by literature (clinical trials etc.). In a second step a data survey was used to collect costs of staff, material and monitoring. Direct medical costs were calculated based on the year 2018 and presented from the payer's perspective. Direct medical costs derived from a number of publicly available sources like outpatient clinic catalogue as well as the DRG catalogue (LKF) and official price lists for the Austrian Health insurances funds.

References

von Minckwitz G et al. N Engl J Med. 2017 Jul 13;377(2):122-131. Marty M et al. J Clin Oncol. 2005 Jul 1;23(19):4265-74. Swain SM et al. N Engl J Med. 2015 Feb 19;372(8):724-34. Verma S et al. N Engl J Med. 2012 Nov 8;367(19):1783-91. Onitilo AA et al. Clin Med Res. 2009 Jun;7(1-2):4-13.
Additional Literature with the author

Results

Additional eBC costs per patient ranged from 14.537€ to 16.352€ per patient (cost differences between groups resulted from differences in recurrence during treatment, adverse effect costs etc). mBC costs avoided by the use of a more efficient regime amounted to 251.917€ per patient.

Fig. 3A: additional eBC costs per patient

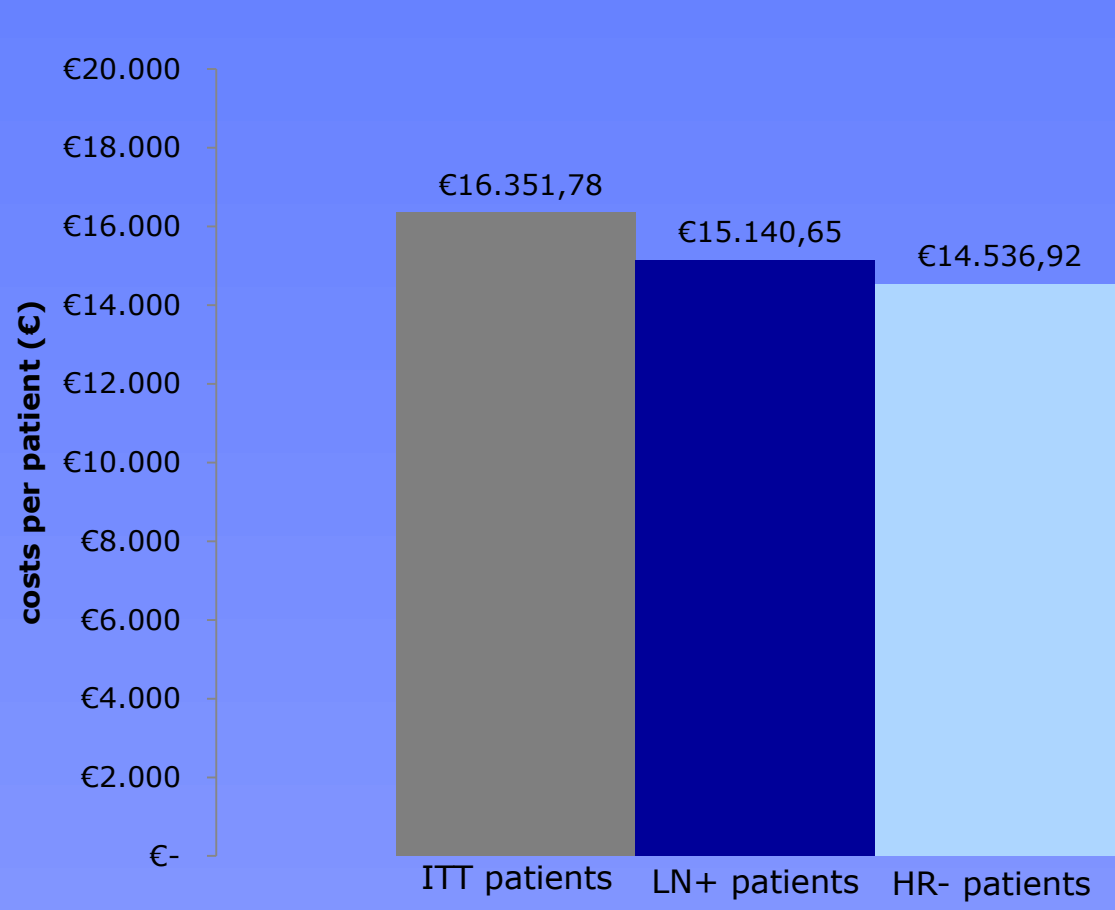
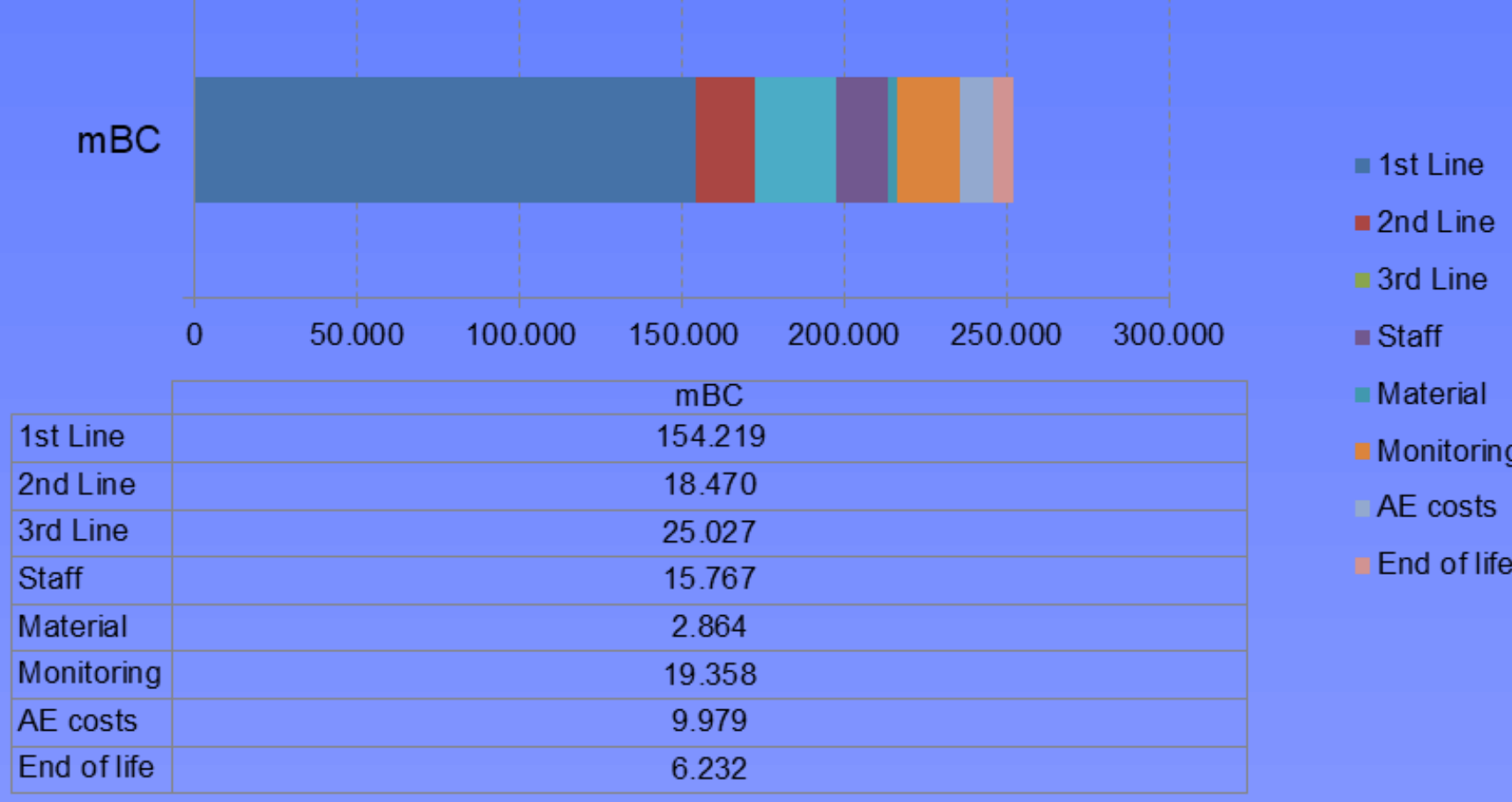


Fig. 3B: avoided mBC costs per patient



Source: own calculations

Based on numbers from Fig. 3A, two analyses were performed. Numbers represent total costs for Austria. Fig. 4A shows the Cost-Benefit Ratio commonly found in calculations such as Cost per QALY gained, assessing the societal willingness to pay. Fig. 4B shows the Budget Impact immediately relevant for payers in the upcoming 5 years.

Fig. 4A: Cost-Benefit Ratio*

*usually performed over the whole lifetime; however here a 5-year frame was chosen due to better reflect the available results of APHINITY

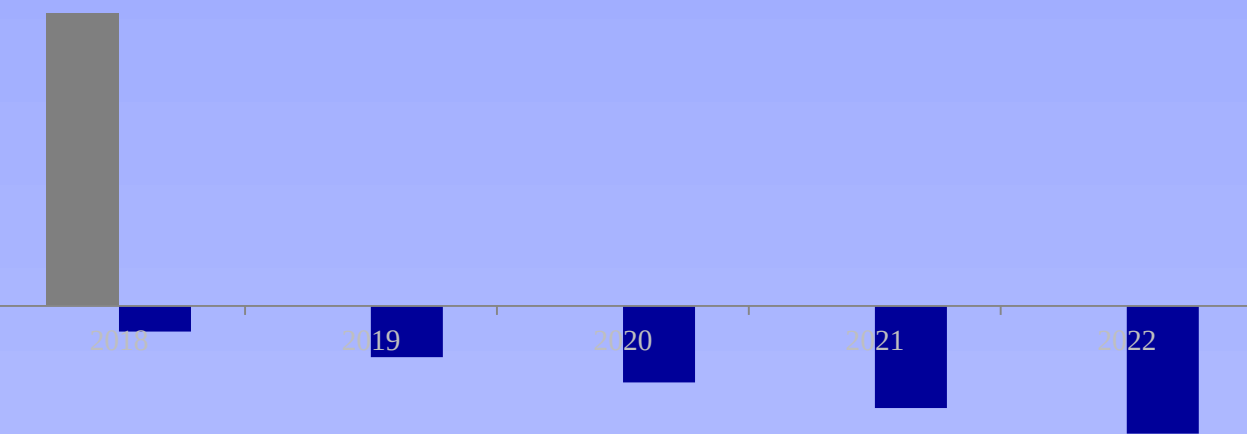
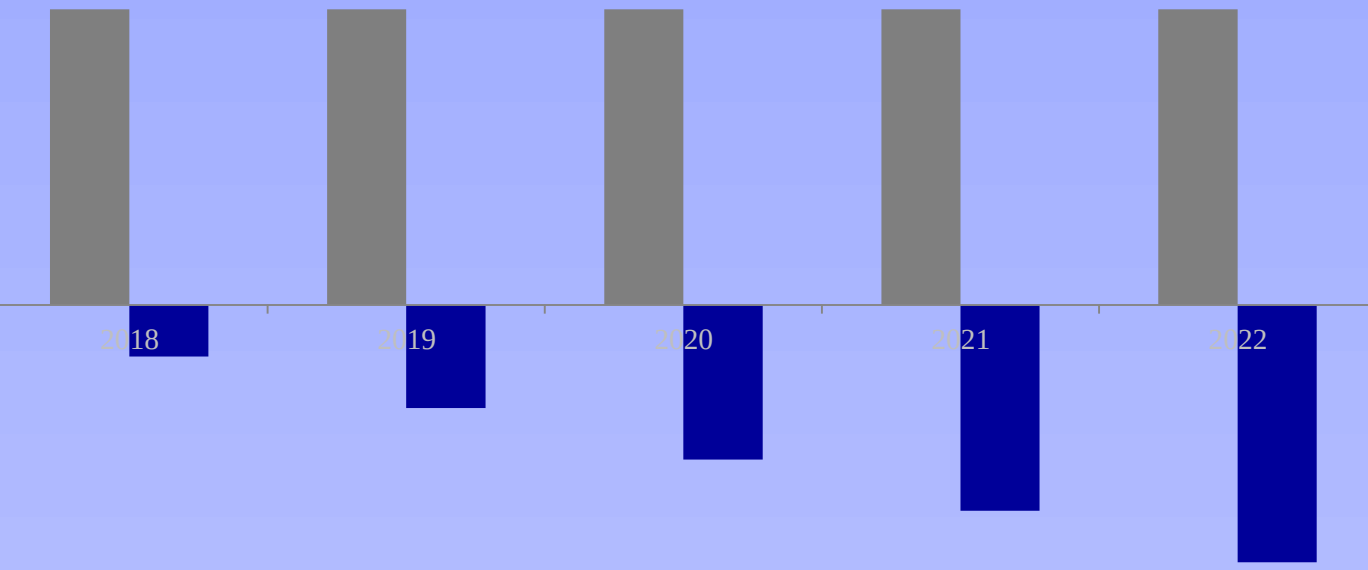


Fig. 4B: Budget Impact



Cost-Benefit Ratio for APHINITY was 2.5 Mio€/year for ITT (0.8% of total hospital medical expenditures, with an associated clinical benefit of 1.7% after 4 years), 0,9 Mio€/year for LN+ (0.3% of costs, 3.2% benefit) and 0,8 Mio€/year for LN- patients (0.2% of costs, 2.3% benefit) (Table 1). Budget Impact amounts to 12.5 Mio€/year in ITT (3.8% of total hospital medical expenditures, with an associated clinical benefit of 1.7% after 4 years), 4.2 Mio€/year for LN+ (1.3% of costs, 3.2% benefit) or 3.9 Mio€/year for HR- (1.2% of costs, 2.3% benefit) (Table 1).

Table. 1: Cost-to-Benefit Ratios (patient based) and Budget-impact results (for the entire cohorts) in Austria

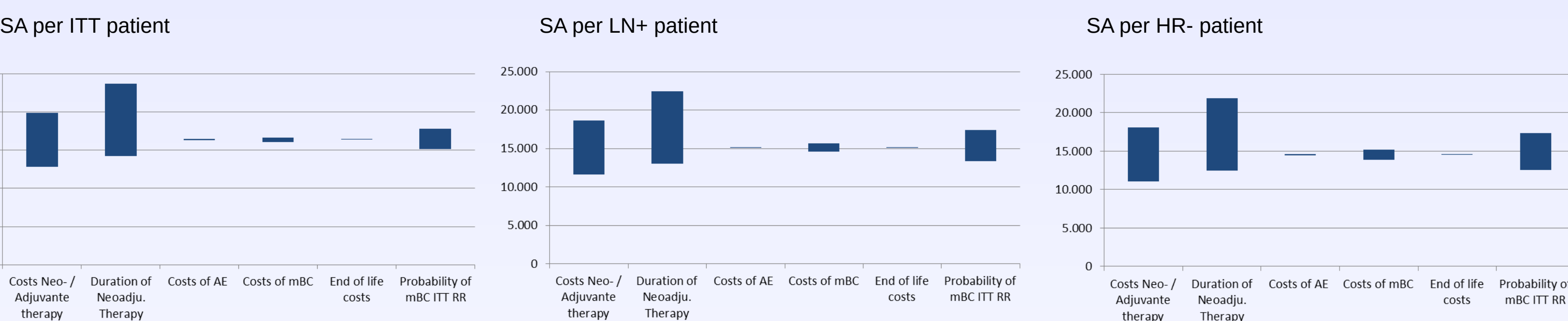
Sub-group	Cost-Benefit Ratio per year in Austria	% of inpatient pharmaceutical expenditures	Budget Impact per year in Austria	% of inpatient pharmaceutical expenditures	APHINITY absolute iDFS benefit for respective subgroup
ITT	2.5 million € / year	0.8 %	12.5 million € / year	3.8 %	1.7 %
LN+	0.9 million € / year	0.3 %	4.2 million € / year	1.3 %	3.2 %
HR-	0.8 million € / year	0.2 %	3.9 million € / year	1.2 %	2.3 %

Source: own calculations

Sensitivity Analysis

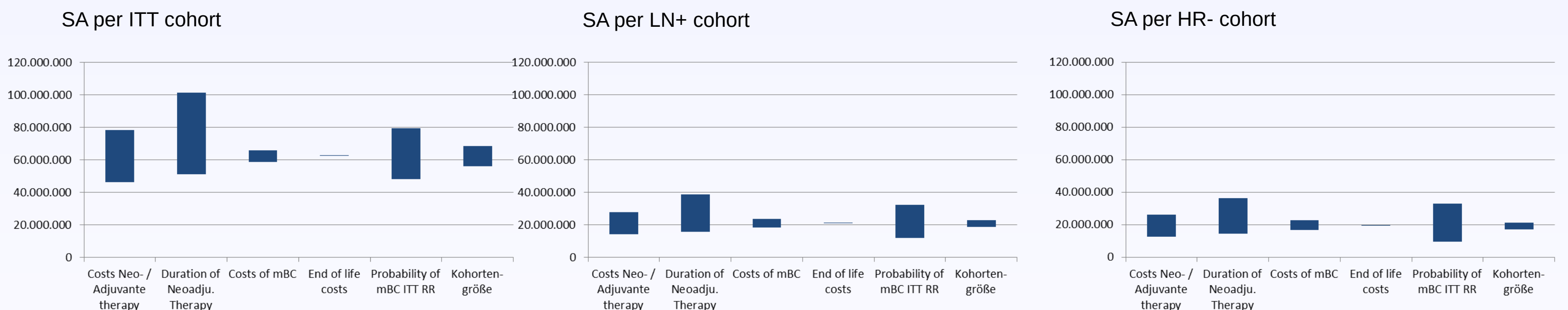
Deterministic sensitivity analysis was carried out in order to assess the impact of variation in the respective variable on the final result. **Fig. 5A** display per patient results (Cost-to-Benefit Ratio calculations) and **Fig. 5B** results for the entire cohorts (Budget-Impact calculations)

Fig. 5A: One-Way deterministic Sensitivity Analysis per patient (Cost-to-Benefit Ratio calculations)



Source: own calculations

Fig. 5B: One-Way deterministic Sensitivity per cohort (Budget-Impact calculations)



Source: own calculations

The highest impact on the results was found to be therapy costs, therapy duration and risk of recurrence.

Conclusion

Adding adjuvant Pertuzumab to SOC would reduce disease-burden with affordable additional expenses.