COST-EFFECTIVENESS OF COMBINATION PERTUZUMAB + TRASTUZUMAB VS TRASTUZUMAB IN HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR 2-POSITIVE EARLY BREAST CANCER (HER2+ eBC) IN THE CZECH REPUBLIC

HTA166

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OBJECTIVES:

Treatment of patients with HER2+ eBC usually involves surgery and radiotherapy, often along with chemotherapy and HER2-targeted treatment before surgery (neoadjuvant/pre-operative therapy) and/or after surgery (adjuvant/post-operative therapy). Patients who achieve complete pathologic response (pCR) after neoadjuvant therapy have better prognosis. Pertuzumab (P) and trastuzumab (H) are humanized monoclonal antibodies, and when combined together, provide a more complete blockade of the HER2 pathway leading to improved pCR rate and longer survival in eBC. The aim of this study was to evaluate cost-effectiveness of the combination pertuzumab and trastuzumab (P+H) compared to trastuzumab (H) in pre– and postoperative setting from payers´ perspective in the Czech Republic.

METHODS:

A Markov model was used with a structure presented on Fig. 1. In pre-operative setting, patients can be treated either by H + chemotherapy or by P + H + chemotherapy. After surgery, patients who achieved pCR, can continue either with H or with P+H. Those, who didn't achieve pCR (non-pCR), are predominantly (90%) treated by trastuzumab-emtansine (T-DM1) or by H alone (10%). After adjuvant treatment, patients can either stay in iDFS (invasive disease-free survival) state, go to non-metastatic recurrence, to metastatic recurrence or die. Main sources of clinical evidence are included in Tab. 1. Demographic characteristics, transition probabilities in iDFS for non-pCR patients and utility values in eBC were derived from KATHERINE trial, which showed superiority of T-DM1 against H in non-pCR patients after surgery[2]. pCR rate of P+H patients was taken from BERENICE trial[4], whereas pCR rate of H patients from HannaH trial[5]. To calculate survival of pCR patients after surgery, EFS (event-free survival) HR of pCR vs non-pCR patients and EFS HR of P+H vs H for pCR patients from Swain et al. 2022[3] were applied on extrapolated iDFS KM curves from KATHERINE trial. The costs for (neo) adjuvant therapies, subsequent therapies, adverse events and other costs were adapted according to the published local costs of 2023. To test robustness of the results, we also conducted alternative scenario analysis with underlying transition probabilities in iDFS for non-pCR patients from Swain et al. 2022[3] (instead of KATHERINE). To determine survival of non-pCR patients treated by T-DM1, we used an EFS HR of T-DM1 vs H from KATHERINE trial.

Tab. 1. Overview of key parameters in the cost-effectiveness

Parameter	BASE CASE	ALT. SCENARIO
Discounting	3%	
Starting age	49	
Time horizon	51 years	
Source of neo EFS	PEONY[1]	
Source of iDFS non-pCR	KATHERINE[2]	Swain et al.[3]
Source of EFS HR of pCR vs non-pCR patients	Swain et al.[3]	
Source of pCR rates	BERENICE[4], HANNAH[5]	
Source of EFS HR of P+H vs H	Swain et al.[3]	
Source of T-DM1 vs H HR	-	KATHERINE[2]
1st line mBC data	CLEOPATRA[6]	
2st line mBC data	CLEOPATRA[6], EMILIA[7]	
Utilities in eBC	Pooled from KATHERINE[2]	
Utilities in mBC	Lloyd et al.[8]	

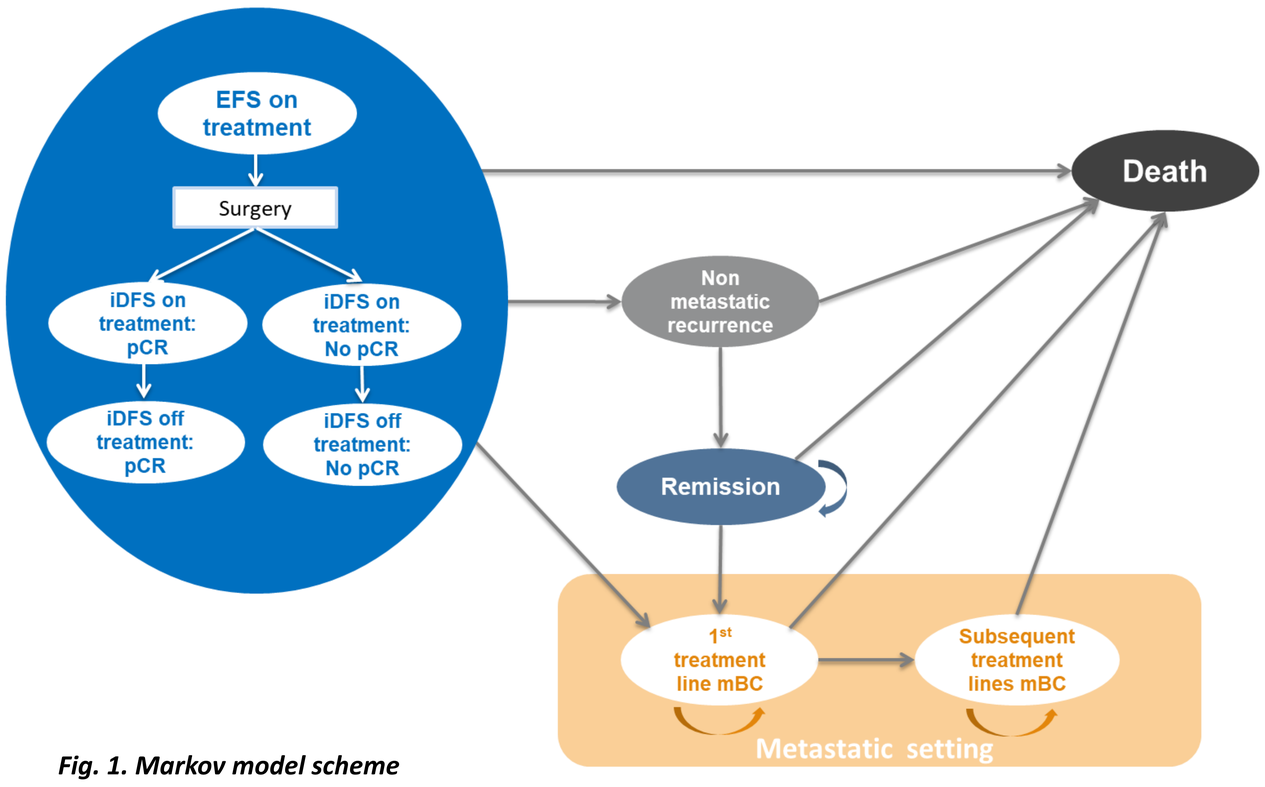

Fig. 1. Markov model scheme

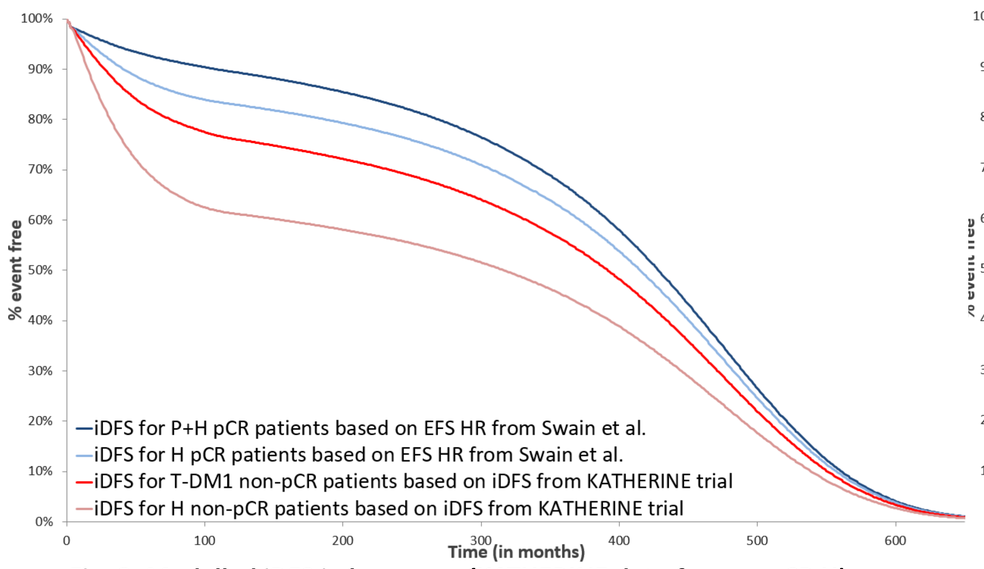

Fig. 2. Modelled iDFS in base case (KATHERINE data for non-pCR H)

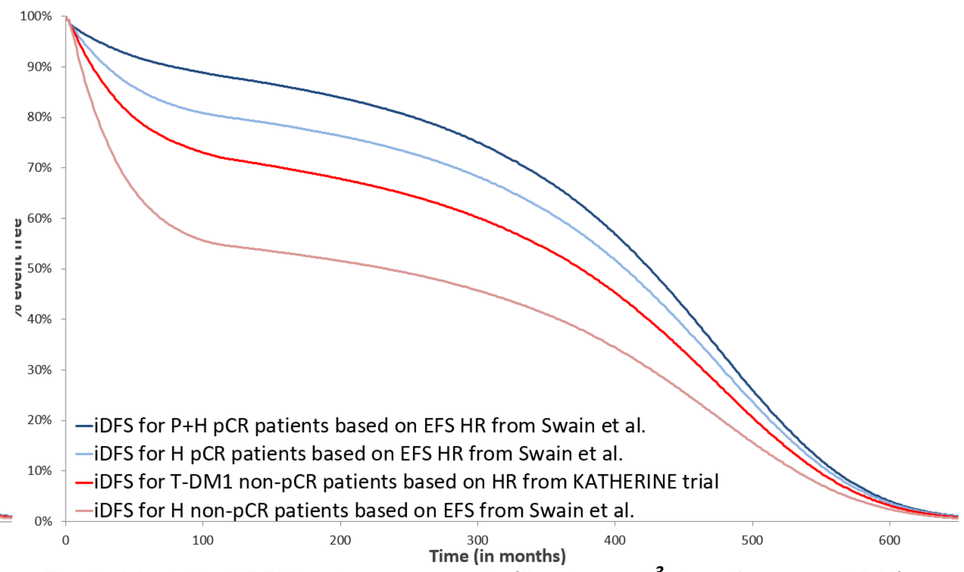

Fig. 3. Modelled iDFS in altern. scenario (Swain et al.[3] data for non-pCR H)

RESULTS:

Over a time horizon of 51 years, P+H generates 0.62 incremental QALYs and 9 909 EUR of additional costs compared to H with ICER 15 966 EUR/QALY in the base case. In the alternative scenario, the QALY gain was even larger with 0.77 incremental QALYs and 7 948 EUR of incremental costs, leading to ICER 10 336 EUR/QALY.

Tab. 2. Results for base case (KATHERINE data for non-pCR H)

BASE CASE		P+H	H	P+H vs H
QALYs	In iDFS	14.59	13.74	0.85
	In non-meta. recurrence	0.02	0.03	- 0.01
	In remission	0.12	0.20	- 0.08
	In metastatic	0.17	0.24	- 0.07
	In metastatic progression	0.16	0.22	- 0.06
	TOTAL QALYs	**15.05**	**14.43**	**0.62**
Costs	Total iDFS cost (EUR)	72 959	50 145	22 814
	Total non-meta. rec. cost (EUR)	365	623	- 259
	Total remission cost (EUR)	64	110	- 46
	Total 1st line mBC cost (EUR)	15 097	21 206	- 4 663
	Total 2nd line+ mBC cost (EUR)	19 450	27 350	- 7 899
	Total EoL cost (EUR)	99	136	- 37
	TOTAL COST (EUR)	**108 035**	**99 571**	**9 909**
Costs/QALY gained				**15 966**

Tab. 3. Results for alternative scenario (Swain et al.[3] data for non-pCR H)

ALTERNATIVE SCENARIO		P+H	H	P+H vs H
QALYs	In iDFS	14.14	13.09	1.04
	In non-meta. recurrence	0.02	0.03	- 0.01
	In remission	0.14	0.24	- 0.10
	In metastatic	0.20	0.29	- 0.08
	In metastatic progression	0.19	0.27	- 0.08
	TOTAL QALYs	**14.69**	**13.92**	**0.77**
Costs	Total iDFS cost (EUR)	72 694	49 454	23 240
	Total non-meta. rec. cost (EUR)	442	759	- 316
	Total remission cost (EUR)	78	134	- 56
	Total 1st line mBC cost (EUR)	13 956	19 517	- 5 561
	Total 2nd line+ mBC cost (EUR)	22 947	32 259	- 9 312
	Total EoL cost (EUR)	119	165	- 46
	TOTAL COST (EUR)	**110 236**	**102 288**	**7 948**
Costs/QALY gained				**10 336**

CONCLUSIONS:

The add-on pertuzumab to (neo) adjuvant therapy has clear clinical benefits with very acceptable incremental costs. This was demonstrated also in the alternative scenario with different data set up. Thanks to the robustness of the results, the Czech HTA agency approved reimbursement of pertuzumab in this indication.

Literature:

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