COST-EFFECTIVENESS ANALYSIS OF NEOADJUVANT PERTUZUMAB THERAPY IN WOMEN WITH LOCALLY ADVANCED, INFLAMMATORY, OR EARLY HER2-POSITIVE BREAST CANCER IN ITALY

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Objective

- The aim of this study was to evaluate the cost-effectiveness of pertuzumab in combination with trastuzumab and docetaxel as neoadjuvant treatment for locally advanced, inflammatory, or early stage breast cancers (BC) that overexpress Human Epidermal growth factor Receptor 2 (HER2), from the Italian National Health System (SSN) perspective.
- Pertuzumab, a novel anti-HER2 antibody, when combined with the HER2-directed antibody trastuzumab and chemotherapy in BC treatment, improves the pathological complete response rate (pCR) [1].
- Patients achieving pCR have high chance to prolong long-term outcomes, as progressive free survival (PFS) and disease free survival (DFS) [2].

Methods

- A six state Markov model [Figure 1] was used to estimate outcomes and costs over a 50-year time horizon (lifetime).
- Patients were assumed to receive standard neoadjuvant therapy containing trastuzumab alone and docetaxel (TD) or the same regimen plus pertuzumab (PTD). After surgical resection, patients receive up to one year of trastuzumab in adjuvant setting and 3 cycles of FEC concomitant therapy (i.e. 5-fluorouracil, epirubicin and cyclophosphamide) (Figure 2).
- Transition probabilities to progressive disease and death were based on total pCR rates observed in the NeoSphere study [1]. A second analysis was carried out in which PFS was directly modelled on observed data [2].
- Female general population mortality rate [3] was applied beyond ten years from BC diagnosis.
- Expected survival was adjusted by utility weights for health states (Table 1) derived from literature [4,5].
- Patients experiencing locoregional recurrence received one year of adjuvant therapy with trastuzumab monotherapy. Metastatic relapse was treated with a first line therapy (i.e. pertuzumab and trastuzumab or trastuzumab monotherapy) followed by a second line (i.e. trastuzumab emtansine or lapatinib and capcitabine) in case of progression. The proportion of metastatic relapse and locoregional was as observed in NeoSphere trial [2] (58% and 42%, respectively).
- Direct medical unit costs were collected from official and published Italian sources, and included drug [6] (Table 2), administration [7], adverse event managing [8] and supportive care costs [7,9] (Table 3). The analyses were run neglecting the discounts on drug prices, both those fixed by national legislation and those negotiated between manufacturers and SSN.
- Costs and health gains were discounted at an annual 3% rate [10].
- Probabilistic sensitivity analysis (PSA) was carried out to evaluate uncertainty.

Results

- Pertuzumab combination is associated with incremental LYs, QALYs and costs (0.40, 0.38 and € 10,479 respectively) relative to standard neoadjuvant regimen. The estimated ICER in the main analysis is € 27,561 per QALY gained (Table 4).
- Acquisition drug cost of pertuzumab is the primary contributor to the difference in costs (Figure 2), partially offset by the prevention of relapse and worsening (Figure 3).
- The PSA substantially confirms the findings of the main analysis (Figure 4). Pertuzumab combination has about 65% of probability of being cost effective relative to standard regimen for a willingness to pay (WTP) threshold of € 40K per QALY gained (Figure 5).
- The ICER of the second analysis performed directly on PFS data is € 13,996 per QALY gained. PSA shows high uncertainty of estimated QALY and cost differences (PTD vs. TD): 0.53 (CI 95%: -2.09; 2.73) and 7.382 (CI 95%: -38.610; 61.567), respectively.
- These analyses can be considered a worst-case, since they were performed using all the least favourable assumptions. In further analyses conducted considering drug prices net of all discounts, the estimated ICERs are even more favourable, in the range € 3,000 - € 19,000.

Conclusions

- BC with HER2 overexpression is associated with increased tumour aggressiveness, higher rates of recurrence and mortality. In the neoadjuvant setting, pertuzumab in combination with trastuzumab and docetaxel is expected to be more effective (increased probability to reach higher pCR rate and longer PFS) than standard regimen, at a favourable cost per QALY gained.

References

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