The high price of anticancer drugs does not reflect therapeutic benefit in Italy

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Background:

The rising price of anticancer drugs is a global concern, with new medicines exceeding 100.000 euros per year of treatment. A previous study conducted in the U.S. highlighted that the price of new drugs did not reflect the patients' benefit [1], demanding for negotiation as potential solution [2]. In Italy – where the price negotiation is mandatory - the hospital drug expenditure in 2016 showed a 13.4% increase over the previous year, with an estimated spending for anticancer drugs of 3.2 billion euros [3].

Objective:

To investigate whether the relative benefit of new anticancer drugs affected their price despite negotiation.

Methods:

Anticancer drugs centrally authorized by the European Medicines Agency (EMA) between January 2011 and May 2016 and approved by the Italian Medicines Agency up to December 2016 were identified. Generics, biosimilars, interferons and G-CSF were excluded. The information on the relative benefit, defined in terms of Overall Survival (OS) and Progression Free Survival (PFS), was extracted from the pivotal trials that compared new treatments with controls, as reported in the European Public Assessment Reports publicly available on the EMA website. The cost of full course, or a 1 year treatment, was estimated from the negotiated ex-factory price published in the Official Gazette of the Italian Republic. A further reduced price was calculated based on additional cuttings compulsory for hospital procurements.

Linear regression was performed to assess the relationships between the improvement in OS or PFS (in weeks) and the negotiated price of anticancer drugs . Adjustment by tumour type was also performed. Sensitivity analyses by tumour type and by control type (i.e. active vs placebo) were planned.

Results:

Overall, 53 anticancer drugs for 67 indications were retrieved. Thirty-five out of 53 drugs (66%) were approved on the basis of pivotal trials using OS or PFS as endpoints. We evaluated the relationship between the improvement in OS (in weeks) and negotiated ex-factory price in 16 drugs (17 indications) and no significant relationship was observed (β= -572.95; P=0.512), with an extremely low correlation coefficient (R2= 0.029). Similar analysis conducted using the PFS (weeks) on 25 drugs (29 indications) also showed no significant relationship (β= -113.52; P=0.738) and no

correlation (R2= 0.004). Repeating the analyses applying the additional price reduction for hospital procurements, or adjusting by tumour type, no improvement in the benefit/price relationships was highlighted. Sensitivity analyses conducted excluding negative values or only using data from the placebo controlled trials did not alter the main findings.

Conclusion:

Our results confirm that the price of anticancer drugs does not reflect their therapeutic benefit. The effect of the negotiation which is mandatory by law in Italy does not balance the system, calling for further efforts in establishing a standard determinant of drug prices. These results merit to be confirmed in other countries where the national price negotiation is in place.

References:

1) Mailankody S, Prasad V. Five Years of Cancer Drug Approvals: Innovation, Efficacy, and Costs. JAMA Oncol. 2015 Jul;1(4):539-40. doi: 10.1001/jamaoncol.2015.0373.

2) Prasad V, De Jesús K, Mailankody S. The high price of anticancer drugs: origins, implications, barriers, solutions. Nat Rev Clin Oncol. 2017 Mar 14. doi: 10.1038/nrclinonc.2017.31.

3) The Medicines Utilization Monitoring Centre. National Report on Medicines use in Italy. January-September 2016. Rome: Italian Medicines Agency, 2017.