Bevacizumab in advanced cancer, too much or too little?

Last year Bernardi et al. [1] said 'By 2008, anticancer drugs will be the leading therapeutic area in term of sales. This appraisal has been done by the Intercontinental Marketing Services (IMS) Health, a provider of business intelligence and strategic consulting services for the pharmaceutical and 'health care' industries. Oncology, considered a niche sector just a few years ago, will reach a business volume of 41 billion dollars in 2008 compared with 24 billion dollars in 2004. The economic aspects will increasingly restrict access to new and expensive oncological drugs (e.g. Targeted therapy as monoclonal antibodies and angiogenesis inhibitors) in different health care realities.'

Today the high economic cost of bevacizumab (Avastin, Roche) is a real problem which involves also mass-media. First of all Reuters on Thursday, 26 June 2008, announced: 'The British National Institute for Clinical Health and Excellence (NICE) said it was unable to recommend first-line use of Avastin in lung and breast cancer after Roche failed to submit clinical and cost effectiveness evidence'. For this reason, Roche’s cancer drug Avastin will not be made available for use on Britain’s state health service because the Swiss drugmaker has refused to provide enough information to assess its cost-effectiveness.

Recently (6 July 2008), the USA web newspaper ‘International Herald Tribune’ wrote about Avastin: ‘Costly cancer drug offers hope, but also a dilemma’.

‘Looked at one way, Avastin, made by Genentech (Roche Partner), is a wonder drug. Approved for patients with advanced lung, colon or breast cancer, it cuts off tumors’ blood supply, an idea that has tantalized science for decades. And despite its price, which can reach $100,000 a year, Avastin has become one of the most popular cancer drugs in the world, with sales last year of about $3.5 billion, $2.3 billion of that in the United States. But there is another side to Avastin. Studies show the drug prolongs life by only a few months, if that. And some newer studies suggest the drug might be less effective against cancer than the Food and Drug Administration had understood when the agency approved its uses.’

Dr Leonard Saltz, a colon cancer specialist at Memorial Sloan-Kettering Cancer Center in New York, said of the new data that ‘the incremental benefit may be more modest than we want to admit’.

‘Then ‘What does it mean to say an expensive drug works? Is slowing the growth of tumors enough if life is not significantly prolonged or improved? How much evidence must there be before billions of dollars are spent on a drug? Who decides? When, if ever, should cost come into the equation?”

A very interesting opinion of Mr Roy Vagelos, a former chief executive of Merck who is considered an elder statesman of the industry, said: ‘… in a recent speech that he was troubled by a drug, which he would not name but which was a clear reference to Avastin, that costs $50,000 a year and adds four months of life. There is a shocking disparity between value and price, and it’s not sustainable’. ‘Cancer drugs constitute the second biggest category of drugs in the United States behind cholesterol-lowering medicines, and accounted for $17.8 billion of total prescription drug sales of $286.5 billion in 2007, according to IMS Health, a health care information company. Spending on drugs for cancer grew 14% last year, faster than for all but three other diseases.’

Avastin example offers an opportunity to improve the methodological aspects: in the report [1] the three levels macro-, meso- and microlevel include the amount of resources that a nation devotes to health care.

What happened in UK was an example of macrolevel decision: no supplement of data by Roche, no authorization for drug use.

In United States, in addition to private insurance, the patients pay 25% of the cost of the treatment, which includes Avastin. This is an example of decision of cooperation between macro- and microlevel to pay the amount of cost. The last possibility (probably an unrealistic one) is that the National health refunds the global expenses. Since 75% of pharmaceutical expenditure is publicly reimbursed in Europe, pharmaceuticals have been subjected to a wide range of pricing policies. In this perspective, important questions emerge: how to face change? Should economic evaluation be integrated with ethical evaluation? Is this achievable?

The problem is serious and it is the first time in the history of Medical Oncology, in industrialized countries, that there are different possibilities for a patient to receive treatment.
Very interesting appears the protocol between Italian Drugs Agency (AIFA) and Roche Italia. The new agreement is on the basis of the identification of an annual maximum cost for patient (medium) in charge of Italian National Health System (SSN) for all the indications independently from Bevacizumab protocol and doses [2]:

1 Identification of an annual maximum cost for patient in charge of the SSN based on the Colon-Recto indication (low dosage for 52 weeks).
2 Identification of the cycle number in charge of the hospital, for year of treatment, in order to maintain the cost of the high dosage schedules in the limits of point 1.
3 Risk sharing to 50% for the first 1.5 months (6 weeks) for all the indications, schedules, dosages and frequency (every 2, 3 weeks).
4 Payback from the company at the end of the treatment.
5 This protocol Roche/AIFA will be in use for 24 months.
6 Otherwise for high dosages and every schedule of Avastin, the agreement defines a cut-off on the basis of bevacizumab dosage approved in colon–rectal cancer, for this reason the reimbursement is on the basis of 5 U/kg (lung, breast and renal cancer)

AIFA has identified the annual maximum cost in charge of the SSN on the base of the treatment of the colon rectal cancer with the avastin dosages (5 mg/kg every 2 weeks) for a patient with a medium weight of 70 kg.

If the treatment exceeds the year, it will be not applied the risk sharing for the first 6 weeks.

In Italy, at the present time, the treatment with Avastin cannot exceed € 25,941 per year, for all approved pathologies.

All economic considerations need to balance the benefits to be obtained with the costs to obtain the benefits.

In our opinion, this protocol AIFA/Roche Italia spa is considered a good start for a promising future in which drug makers and National Health cooperate for a cost reduction but also for a better treatment in patients with low life expectancy.

A. Jirillo1*, F. Vascon1 & M. Giacobbo1

1Department of Medical Oncology, Istituto Oncologico Veneto IOV, IRCCS, Padova, Italy
(*E-mail: jirillo@libero.it)

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