**Round table no. 7**

# Assessment of anti-cancer drugs for reimbursement: methodology, relation between effectiveness and therapeutic needs

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## "NO PREMIUM FOR ANTI-CANCER DRUGS"

Between effectiveness and therapeutic need, do anti-cancer drugs have any particular specific characteristics? Must we consider anti-cancer drugs as a cultural exception? Are they drugs just like any other? The recent decision on the insufficient medical benefit provided by an anti-cancer drug resounded like a clap of thunder out of a clear blue sky. This issue was therefore highly topical this year in Giens, where industry decision-makers and the authorities come together for an exchange of views.

There is no premium on an anti-cancer drug because this is a serious disease. In spite of everything, the degree of effectiveness enters into the definition of the level of improvement in medical benefit. Nowadays, however, this criterion alone may be considered too weak and result in a lower level of reimbursement by the health insurance agency. It is therefore not necessarily unreasonable to assess the improvement in medical benefit of anti-cancer drugs as insufficient. Our group had some lively exchanges on the various efficacy criteria, in an attempt to identify their relative importance and their limitations. From our deliberations, it emerges that overall survival is not always the ideal main criterion. Some cancers require much longer monitoring, with multiple therapeutic lines that, fortunately, do not necessarily end in the death of the patient. We therefore need intermediate or substitute criteria. Survival without progression of the disease is interesting to take into consideration, but halting the progress of the disease does not necessarily lead to survival. These various appreciations still pose problems, and we set aside the advantages and disadvantages to focus instead on the limitations of the criteria currently being used. Overall survival, survival till progression and disease-free survival remain the fundamental criteria. Our group felt it would be useful to eliminate certain other criteria deemed of little value, such as time to treatment failure and response rates, except in the case of haematological cancers. There was much debate as to the importance of considering these survival analyses. We need graphs, but how best are we to interpret them given that

median survival has its limitations? We found it extremely interesting to discuss these rules and the various criteria already presented in studies, with their limitations and constraints. The definition of effectiveness and how it is expressed seems to pose an obstacle to understanding. Determining a threshold of effectiveness for the granting of reimbursement status remains difficult, since it depends on the therapeutic need for the comparator used. Overall, it is tolerance that weights the assessment of the product's therapeutic contribution. Thus the huge increase in new predictive factors of response such as biomarkers or histology is creating a tendency towards smaller target populations by defining sub-groups where the expected effectiveness may prove much higher.

We also identified some problems with the comparators, which evolve very quickly in cancerology. With over 700 molecular entities currently in development, everyone wants to work on cancer, and the strategies we rely on for starting a clinical trial today will not necessarily be valid in two years' time. In addition, new biomarkers are being discovered every day. The pharmaceutical industry is trying to identify markers for the efficacy of their products in order to select the populations that will or will not respond. This work may remain purely prospective and studies last up to three years in order to gauge the level of response in given populations. The analyses by sub-group that will be provided for in the protocol are open to discussion as regards methodology. This work is not always properly recognised, however. When greater effectiveness is noted in a sub-population, which responds better to a marker in certain types, it should be possible for the Transparency Commission to make a satisfactory assessment conditional on the decision being confirmed by other studies.

Given the uncertainties, the round table suggested the possibility of issuing a temporary improvement in medical benefit decision which would then be subject to confirmation by the Transparency Commission.