A LOSS OF CHANCE INDEX: A NEW TOOL FOR OPTIMIZING PATIENT ACCESS TO INNOVATIVE DRUGS

François Gavini, MD[1], François Sarkozy, MD[2], Chrystel Jouan-Flahault, MD[3], Pierre Fumoleau, MD[4]

[1] Roche France SAS Boulogne-Billancourt; [2] FSNB Health & Care Paris; [3] LEEM Paris; [4] Centre Georges-François Leclerc, Dijon

Early patient access for innovative drugs in oncology might help preventing a substantial number of progressions and deaths. Estimating the Absolute Loss Of Chance (ALOC) might support patient access decision making process

BACKGROUND

In France, the HAS (Haute Autorité de Santé) is in charge of Health Technology Assessment (HTA) as a basis for Pricing and Reimbursment (P/R) decision. HTA is associated with a time-lag after MA. An almost unique Temporary Use Authorisation (TUA) process allows patients having early access to innovative drugs prior to the P/R decision in specific situations (drugs targeting unmet medical needs) and is formally approved by French RA (ANSM). It aims at reducing the patient loss of chance and filling the time-lag gap between European Marketing Authorisation (EUMA) and French P/R Decision (FPRD). The formal TUA decision may be supported by analytical decision making tools.

OBJECTIVES

Our objectives were to report time-lags between European Marketing Authorisation (EUMA) and French Pricing and Reimbursement Decision (FPRD) for recent innovative anti- solid cancer drugs and to quantify the corresponding potential patient loss of chance and to propose an analytical tool to support decision making.

METHODS

Selection of drugs and data retrieval

We included all cancer drugs approved for solid tumours in Europe in 2011 and 2013. Dates were retrived from the EMA database and Transparency Committee (TC) reports were downloaded from the HAS website with the corresponding Added Medical Value (*Amélioration du Service Médical Rendu* - ASMR), drug indications, the size of target patient populations and basic key data issued from the analysis of pivotal trials. We excluded all drugs with no therapeutic gain (AMV* Level 5).

ALOC calculation

The Number Need to Treat (NNT) to avoid one event (death/progression) was calculated in comparison to the standard treatment for each cancer drug using ph. III RCT data. We assumed efficacy of the new treatment not varying over time and effect size observed in RCT applicable in a real world setting. The number of patient-months "exposed" to access-lag time based was assessed over target population and time-lag period. Where median times to event were short compared to time-lag, a correction of the length of exposure was applied considering patients not being "exposed" for the entire time-lag period.

The ALOC for patients was defined by dividing the number of patient-months "exposed "to access time-lag as a measure of the absolute potential impact unless alternative access (TUA, Clinical Trial …).

Sensitivity analyses

Target populations were defined by the HAS TC based on incident cases without considering patients in the indication at the time of market access (prevalent cases). A sensitivity analysis was performed adding those prevalent cases by additionally considering half of the patients from the HAS TC-based target population size.

*AMV levels,set by the HAS TC, assesses the Added Medical Value (AMV) of the new drug in comparison with existing drugs or strategies for the same indications. It has five levels: 1 = *major*, 2 = *important*, 3 = *moderate*, 4 = *minor*, and 5 = *absence of therapeutic gain*.

RESULTS

Twelve drugs for solid tumours were granted European MA with no clear relationship between Year of MA and time to market access neither between Year of MA and AMV.

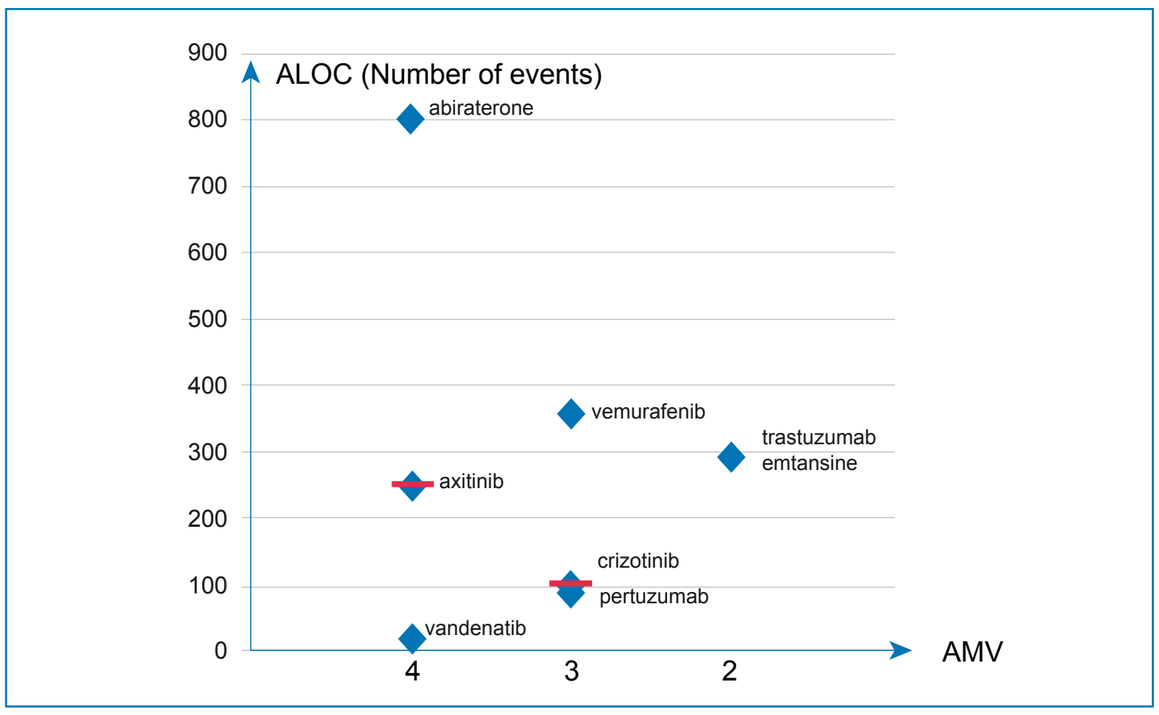

Figure: ALOC (number of progressions and deaths) according to AMV

Population size: mean between TC inferior and superior limits
AMV: Added Medical Value – **ALOC:** Absolute Loss Of Chance
Horizontal bar: median

Among drugs that were granted MA by the EMA between 2011 and 2013, AMV levels ranged from 2 to 4. One drug, trastuzumab emtansine, had an AMV level 2 (important), five drugs had an AMV level 3, and six drugs had an AMV level 4. Time-lag between EUMA and FPRD ranged 7.4 (enzatulamide) to 29.9 months (cabazitaxel). The overall ALOC ranged from 9 to 799 events (20 to 1408 for sensitivity analyses) that may have occur unless alternative access as TUA or CT.

CONCLUSION

- **At the French level, the TUA demonstrated its efficiency against Loss Of Chance because TUA process allows drug dispensation (under French RA control), whilst the regulatory and the pricing and reimbursement process are ongoing; Decision process may include a formal assessment using analytic tools such as the ALOC index based on 'Easy to get' parameters.**
- **For countries where market access takes a significant time from market authorisation, the ALOC index might also be useful as a potential loss of chance indicator for market access timing decision making. This may be an interesting compromise between rapid assessment for market access and in depth assessment for complete Health Technology Assessment.**