ACCEPTANCE OF INDIRECT COMPARISONS IN THE GERMAN EARLY BENEFIT ASSESSMENT

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Objectives

Since 2011, newly marketed drugs undergo an early benefit assessment (EBA), in which the drug's additional benefit (AB) compared to an appropriate comparator (AC) defined by the Federal Joint Committee (GBA) is assessed. Often, there is no evidence available from head-to-head studies with the AC. In such cases indirect comparisons (IC) may be used to prove an AB against the AC. To investigate the acceptance of IC to demonstrate an AB, EBA were retrospectively analyzed.

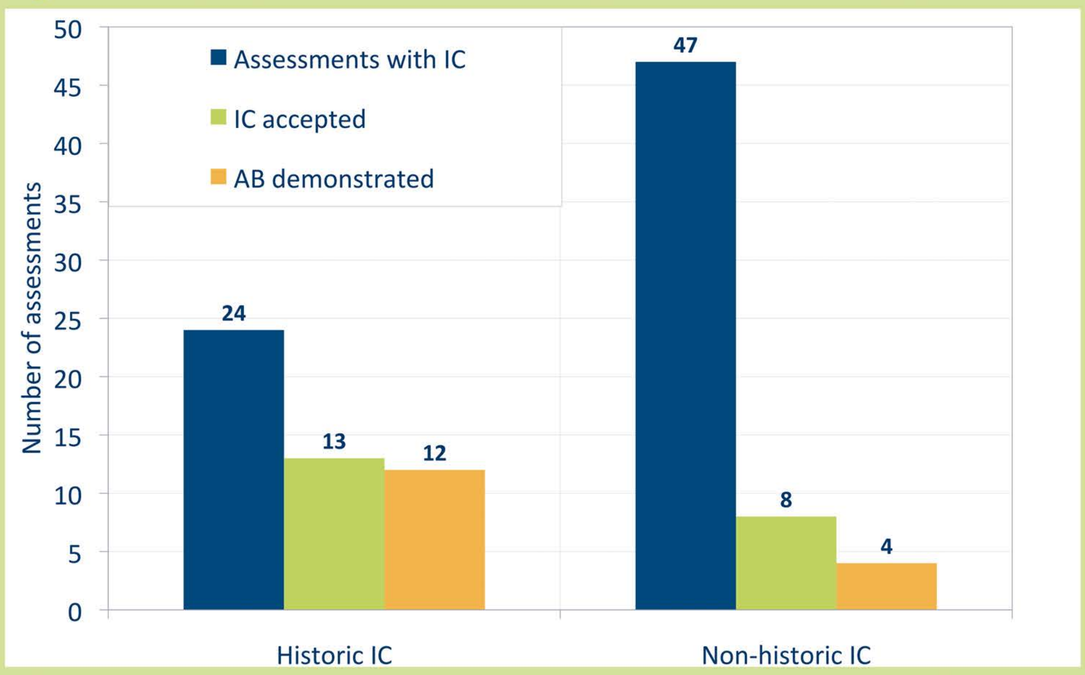
Methods

All EBA until January, 5th 2017 were considered in this analysis. The reasons for the passed resolutions („Tragende Gründe") published by the GBA were screened for keywords („indirekt", „historisch") to preselect potential assessments. Relevant assessments were examined regarding the type of IC (historic i.e. unadjusted vs. non-historic i.e. adjusted), outcome (IC accepted, AB), and reasons for IC rejection by GBA (if applicable) in each assessed patient population.

Results

A total of 82 assessments were identified during the keyword screening, of which 68 included an IC for at least one patient population. 24 assessments contained historic IC, of which 13 were accepted and 12 resulted in an AB (mostly drugs for the treatment of chronic hepatitis C). In contrast, 47 assessments contained non-historic IC, of which only 8 were accepted and 4 resulted in an AB. Hence, only a small proportion of assessments with an IC resulted in an AB (Figure 1).

Figure 1: Overview of assessments with IC



Considering the 21 assessments with accepted IC, both historic and non-historic, a dominance of several therapeutic areas is detectable:

- 10 assessments regarding infectious diseases
- 4 assessments regarding metabolic diseases
- 3 assessments regarding oncological diseases
- and 1 assessment in each of the following therapeutic areas: cardiovascular diseases, eye diseases, diseases of the nervous system, and other diseases.

Within the therapeutic area "infectious diseases", the proportion of chronic hepatitis C is extremely high (9 of 10 assessments) (Figure 2).

Figure 2: Distribution of therapeutic areas regarding accepted IC

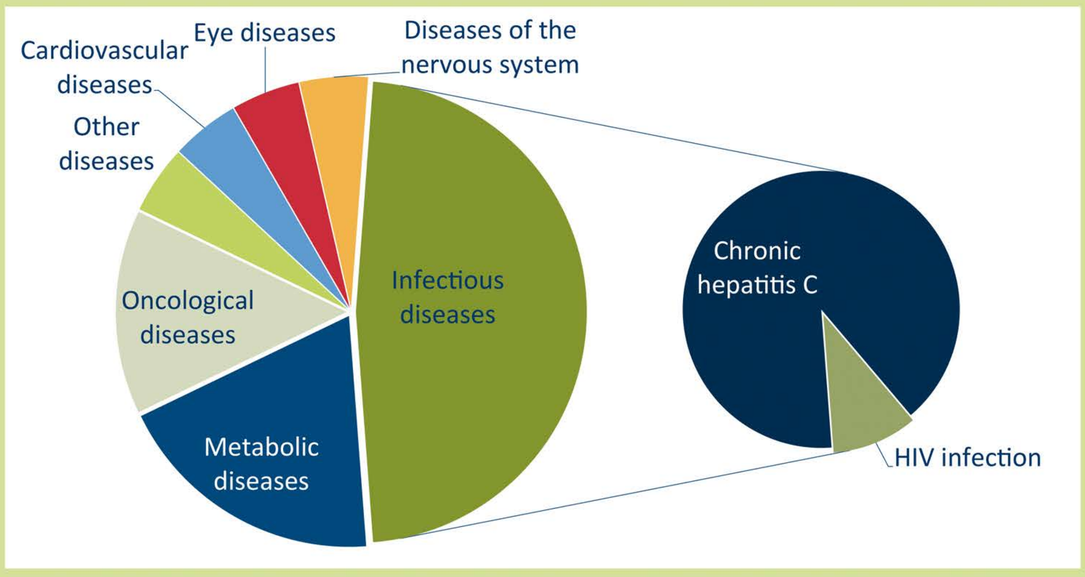


Table 1 shows the extent of the AB and number of affected patient populations by therapeutic area.

Table 1: AB regarding different patient populations

Therapeutic area	AB (number of affected patient populations)*
Historic IC	
Oncological diseases Number of assessments: 3 Number of patient populations: 5	Not quantifiable (4) Minor (1)
Infectious diseases Number of assessments: 7 Number of patient populations: 31	Not granted (4) Not quantifiable (1) Minor (23) Considerable (3)
Other diseases Number of assessments: 1 Number of patient populations: 2	Not quantifiable (2)
Metabolic diseases Number of assessments: 2 Number of patient populations: 2	Not quantifiable (2)
Non-historic IC	
Cardiovascular diseases Number of assessments: 1 Number of patient populations: 2	Not granted (1) Not quantifiable (1)
Metabolic diseases Number of assessments: 2 Number of patient populations: 2	Not granted (1) Minor (1)
Eye diseases Number of assessments: 1 Number of patient populations: 1	Not granted (1)
Infectious diseases Number of assessments: 3 Number of patient populations: 4	Not granted (1) Minor (1) Considerable (2)
Diseases of the nervous system Number of assessments: 1 Number of patient populations: 1	Not granted (1)

*Partly, drugs cover several patient populations. This analysis shows exclusively patient populations for which an IC was provided.

In many assessments, the GBA stated several different reasons for the rejection of IC. Most IC were refused by the GBA due to the following methodological issues (sorted by frequency of naming):

- inappropriate patient populations
- inappropriate statistical methods
- inappropriate bridge comparator
- incomplete study pools
- inappropriate study population
- inappropriate dosage
- inappropriate literature research

Other reasons (not concerning methodological issues) for rejection were:

- deviant AC or inappropriate implementation of AC
- data issues (lack of data, inconsistency, aggregation, plausibility)

Conclusions

It seems reasonable to plan pivotal studies not only to comply with the requirements for marketing authorization but also with the rules of the EBA. Further promotion of the IC methodology accepted by the GBA is recommended as this may improve the chances to have an AB granted.

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References

Gemeinsamer Bundesauschuss: Tragende Gründe zum Beschluss des Gemeinsamen Bundesausschusses über eine Änderung der Arzneimittel-Richtlinie (AM-RL), https://www.g-ba.de/informationen/nutzenbewertung/ (depending on respective EBA)