PARTICIPATION OF EXTERNAL MEDICAL SOCIETIES IN THE BENEFIT ASSESSMENT OF PHARMACEUTICALS IN GERMANY

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Objectives

Every new molecule entity undergoes a benefit assessment by the Federal Joint Committee (G-BA) in Germany, the so called early benefit evaluation. After an assessment of the dossier by the Institute for Quality and Efficiency in Health Care (IQWiG) or the G-BA, external experts can comment during an appraisal process. This research aims to explore how specific external experts (medical societies (MS) and the Drug Commission of the German Medical Association (AkdÄ)) differ from the opinion of the assessment and whether the G-BA agrees or disagrees with them regarding additional benefit, the appropriate comparator and endpoints in its final appraisal.

Methods

All 136 benefit assessments regularly completed between January 2011 and August 2015 were systematically reviewed. The AkdÄ handed in 48 statements. 60 medical societies handed in 232 statements for 112 benefit assessments.

It was determined if MS and AkdÄ recommended a higher, lower or equal additional benefit, relevant to the patient, compared to the assessment. Regarding the appropriate comparator, against which new pharmaceuticals are assessed, experts' agreement or disagreement with the choice in the assessment was determined. Endpoints, which measure the additional benefits, were evaluated (agree/ disagree) when at least one expert disagreed with the assessment.

Results

High degree of controversy regarding additional benefits, appropriate comparators and endpoints. Continuing interest to participate in the process.

Figure 1: Proportion of assessments with statements in the investigated categories

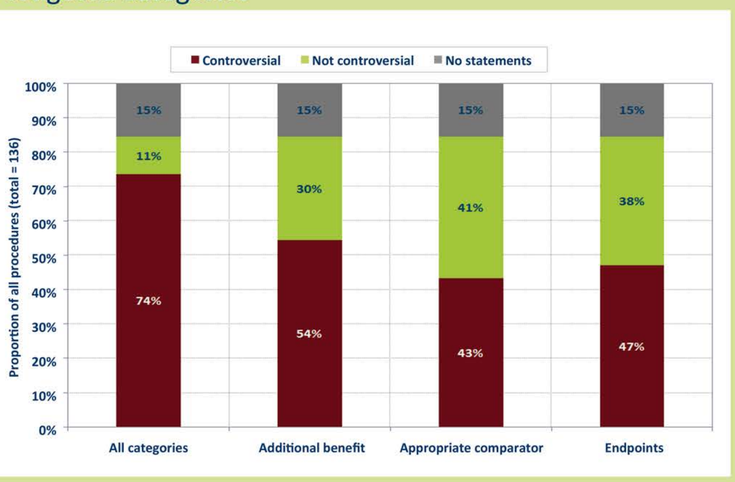
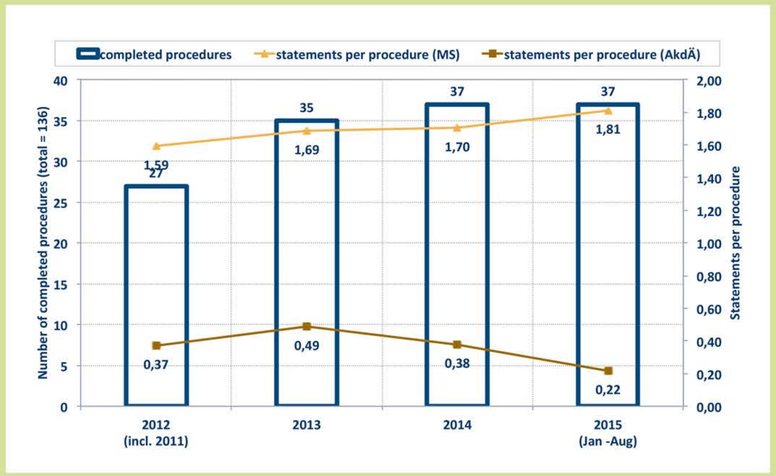


Figure 2: Statements per procedure from 2011 to 2015

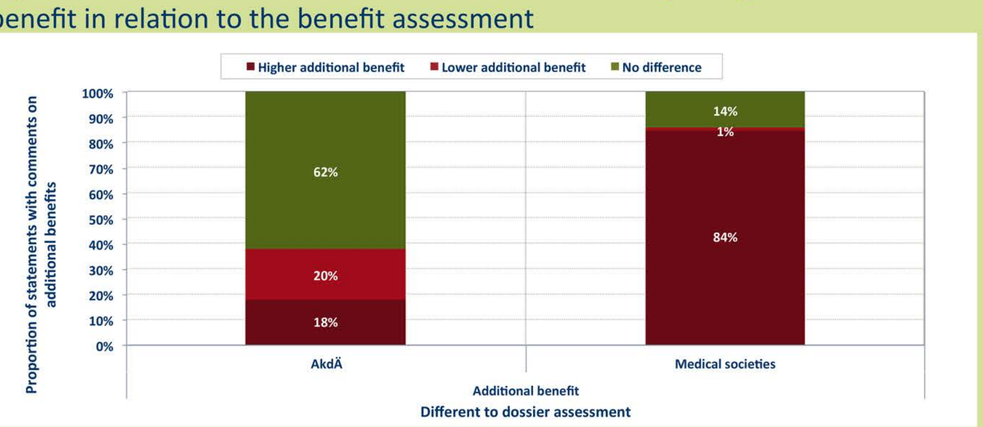


Controversial: At least one position is different to the assessment; Not controversial: In agreement with the assessment or no opinion provided in the statement

Figure 1 gives an overview how often the analyzed categories were discussed by the external experts. In 21 of 136 assessments neither the AkdÄ nor a MS handed in a statement. In 100 assessments at least one of the external experts had a differing opinion in regard to one of the three investigated categories. The external experts had the most objections about the additional benefit (74/136) compared to the recommendations of the benefit assessment. In 64 assessments at least on external expert had a differing opinion regarding the consideration of an endpoint and in 59 assessments an external expert found the benefit assessment controversial with regard to the appropriate comparator. Figure 2 shows that MS have a growing interest in participating in the evaluation process. In 2011/2012 1.6 statements per procedure were handed in. In the first half of 2015 the rate was 1.8.

Medical societies see higher additional benefits than the IQWiG and the AkdÄ

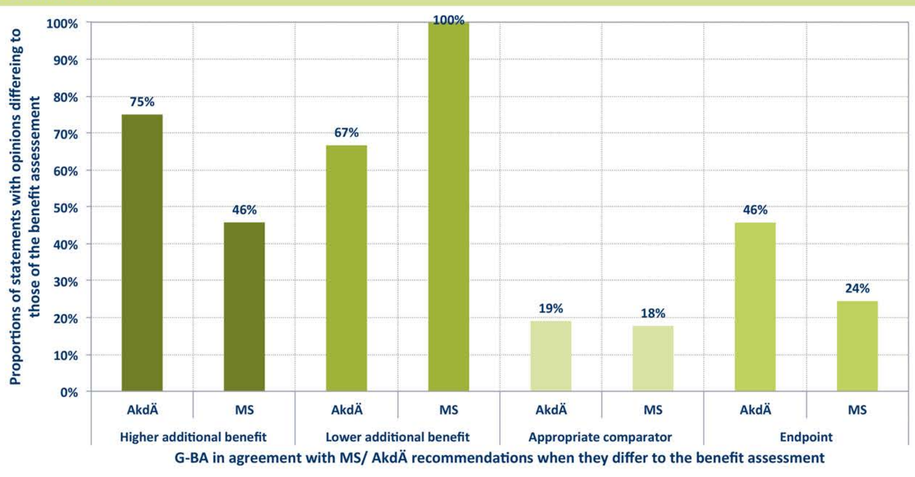
Figure 3: Position in the statements of MS and AkdÄ regarding additional benefit in relation to the benefit assessment



The additional benefit was the most controversial discussed category. Figure 3 shows the leading direction of the opinions of the MS and the AkdÄ. The MS recommended a higher additional benefit significantly more often (118/140) than the AkdÄ (8/45). When the AkdÄ advanced an opinion on the additional benefit it agreed with the benefit assessment (28/45) in most cases. In 9 statements the AkdÄ recommended a lower additional benefit. The MS recommended that only twice. In once case, a MS argued that the considered studies in the assessment were not suitable because of unethical inclusion criteria for the patients. In the other case the IQWiG saw a major additional benefit (highest possible category) for patients over 75 years. One medical society disagreed because in their opinion the quality of life data showed no significant advantage for the new drug.

The G-BA agrees with the AkdÄ more often than with the medical societies in all three categories

Figure 4: G-BA in agreement with MS/ AkdÄ when they differ to the benefit assessment



It is interesting to see if the G-BA comes to similar conclusions as the experts. Figure 4 shows for the different categories if the G-BA agrees with the differing recommendation of the experts. It is important to point out however that an agreement does not imply a casualty between statement and decision of the G-BA but only a equal direction in the opinion compared to the benefit assessment. When MS/ AkdÄ recommended a higher benefit, the G-BA accorded with 54/118 respectively 6/8 of all statements. In case of a lower benefit the rate was 6 out of 9 for the AkdÄ. In case of the two statements of the MS, the IQWiG had recommended high benefit level for specific subgroups within therapeutic areas. The G-BA decided on one low benefit level for the whole area. Hence, the G-BA differed in the same direction as the MS. Regarding the appropriate comparator, the concurrence rates were only 14/79 respectively 4/21. This relatively low rate is not surprising because the G-BA defines the AC before the submission of the dossier. Consequently, an agreement with a differing opinion implies an deviation from its own original opinion. In case of controversial endpoints, the G-BA agreed more often with the AkdÄ (16/35) than the MS (33/135). Progression-free survival (PFS, 28 statements) and objective response/remission rates (ORR, 20 statements) for cancer therapies were the most discussed endpoints. The G-BA declines both because PFS and ORR are combined endpoints, and additionally endpoints based on imaging techniques or laboratory values not accepted. The G-BA prefers overall survival (OS) as a patient relevant endpoint.

Conclusions

The German early benefit evaluation was implemented to generate objective information about the benefit of a drug. All parties participating in the process base their decisions on the same data and use evidence-based medicine methods. However, the high number of divergent opinions between assessment, medical experts and final appraisal demonstrate the need for discourse. The authors recommend different instruments to improve the process. Firstly, medical experts should be involved in the choice of the appropriate comparator . Secondly, they should receive an earlier access to the handed in dossiers. Thirdly, there should be greater transparency towards considered external opinions by the G-BA. The G-BA is obligated to publish a concluding documentation about all statements but many evaluations (62/136) missed such a document when the study here was undertaken. Fourthly, medical experts should be included as voting members of the appraisal board of the G-BA.

This study was funded by Takeda Pharma Vertrieb GmbH & Co. KG.