IMPLICATIONS OF THE FAST EVOLVING THERAPEUTIC LANDSCAPE ON APPROPRIATE COMPARATORS IN ONCOLOGICAL AMNOG BENEFIT ASSESSMENTS

PCN236

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Background

- In the course of the mandatory benefit assessment of new drugs in Germany (AMNOG), an appropriate comparator is defined by the Federal Joint Committee (FJC).
- The appropriate comparator can be categorized into 4 classes: (1) one specific drug; (2) a list of drugs; (3) patient individual therapy; (4) best supportive care (BSC). For the option "a list of drugs" the pharmaceutical companies are free to choose one specific drug as an appropriate comparator.
- To have an added medical benefit granted by the FJC, it is essential for pharmaceutical companies to provide comparative evidence against the appropriate comparator.
- According to the FJC's procedure, six categories for an added medical benefit can be assigned: major, considerable, minor, none, less, and non-quantifiable. Non-quantifiable added medical benefit can be used if the underlying evidence is highly biased and/or decision uncertainty is high.

Objective and Methods

- The aim of the study was to evaluate the pattern of the appropriate comparator assignments as well as the outcome of the assessments over time since the enactment of AMNOG.
- Oncological indications were depicted for this analysis since they represent the majority of all benefit assessments.
- Information was retrieved from all non-orphan Pharmaceuticals Market Reorganization Act (AMNOG) dossiers in the field of oncology published on the FJC website (https://www.g-ba.de) until the end of 2017.
- Information regarding indication, line of therapy, and outcomes was obtained. In addition, it was determined if the comparator used in the relevant clinical trials was accepted as appropriate by the FJC.

Results

- 92 AMNOG dossiers in the field of oncology were published between 2011 and 2017 that were conclusively assessed by the FJC. These dossiers included 172 separately evaluated labels and sub-labels.
- The assignment of appropriate comparators, when considering all assessments by the end of 2017, was distributed as follows: 38 (22%) specific drug; 64 (37%) list of drugs; 31 (18%) patient individual therapy; and 39 (23%) BSC (**Figure 1**).
- The most commonly assigned appropriate comparator was a list of drugs (37%) (**Figure 1**).

Figure 1. A List of Drugs is the Most Commonly Assigned Category of Appropriate Comparators

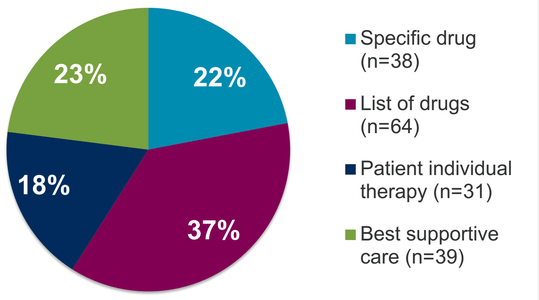
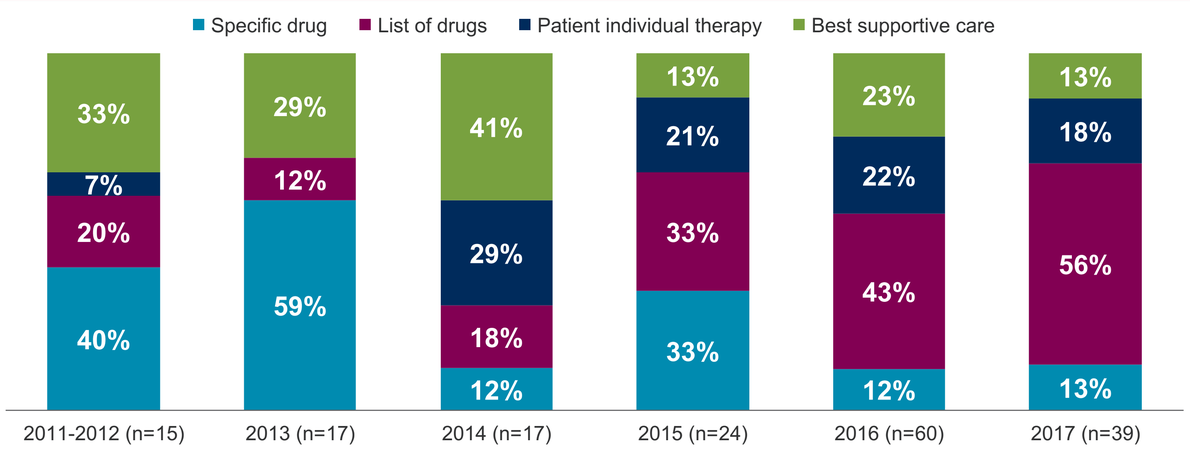
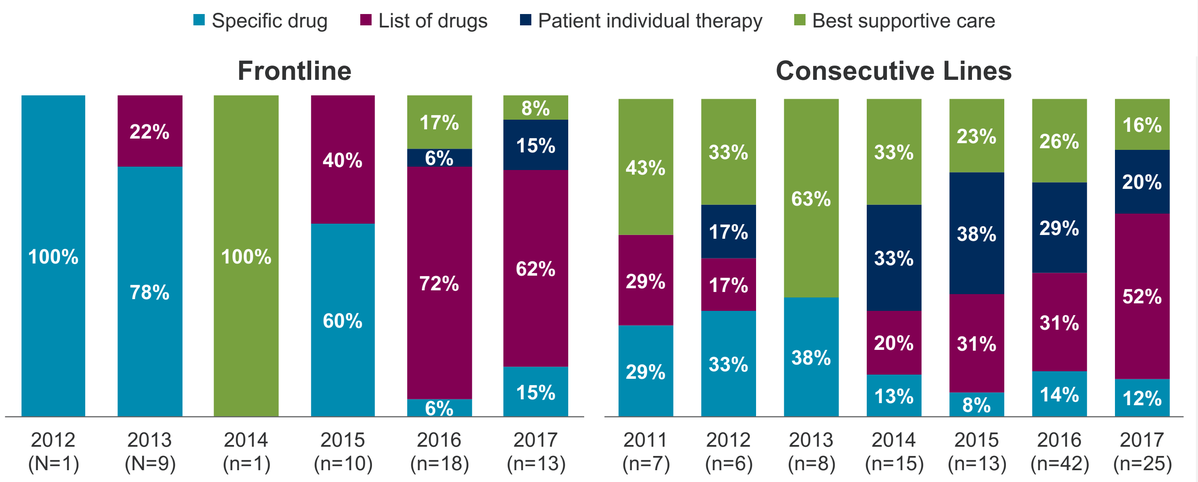


Figure 2. The Pattern of the Appropriate Comparator Assignment Changed over Time



- In the early years of AMNOG (2011-2012) a specific drug was the most frequently assigned category of the appropriate comparator (40%) (**Figure 2**). Subsequently, a significant shift towards a list of drugs occurred. This was most obvious in 2017 where more than half (56%) of the AMNOG-benefit assessments defined a list of drugs as the appropriate comparator (**Figure 2**).
- The categories BSC and patient individual therapy showed higher variability over time, but did not play a major role during the last three years (**Figure 2**).

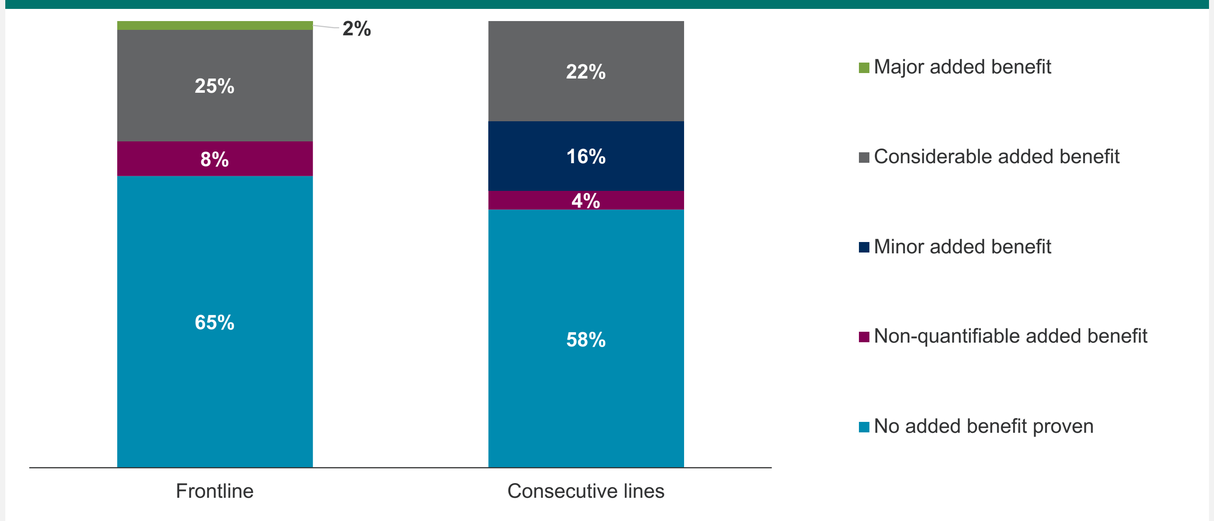
Figure 3. The Appropriate Comparator Assignments Differ Between Therapy Lines



- In total, there have been fewer benefit assessments in the frontline therapy setting compared to the consecutive therapy setting (**Figure 3**).
- In frontline therapies, a list of drugs replaced one specific drug as appropriate comparator. This might reflect the evolution of various new therapy options in the frontline setting, which are deemed equally appropriate by the FJC (**Figure 3**).
- In consecutive therapy lines, patient individual therapy and a list of drugs became more frequently assigned appropriate comparators starting in 2014 and superseded a specific drug. In fact, a list of drugs was the predominantly assigned (52%) appropriate comparator in 2017 (**Figure 3**).
- BSC was less commonly assigned as appropriate comparator in consecutive lines in recent years (2014: 33% vs. 2017: 16%). Since BSC is the preferred comparator therapy for indications lacking curative treatment options, this development reflects the recently increased availability of curative treatments in later treatment lines (**Figure 3**).
- In 2017, the pattern of appropriate comparator assignment converged between front and consecutive therapy lines (**Figure 3**).

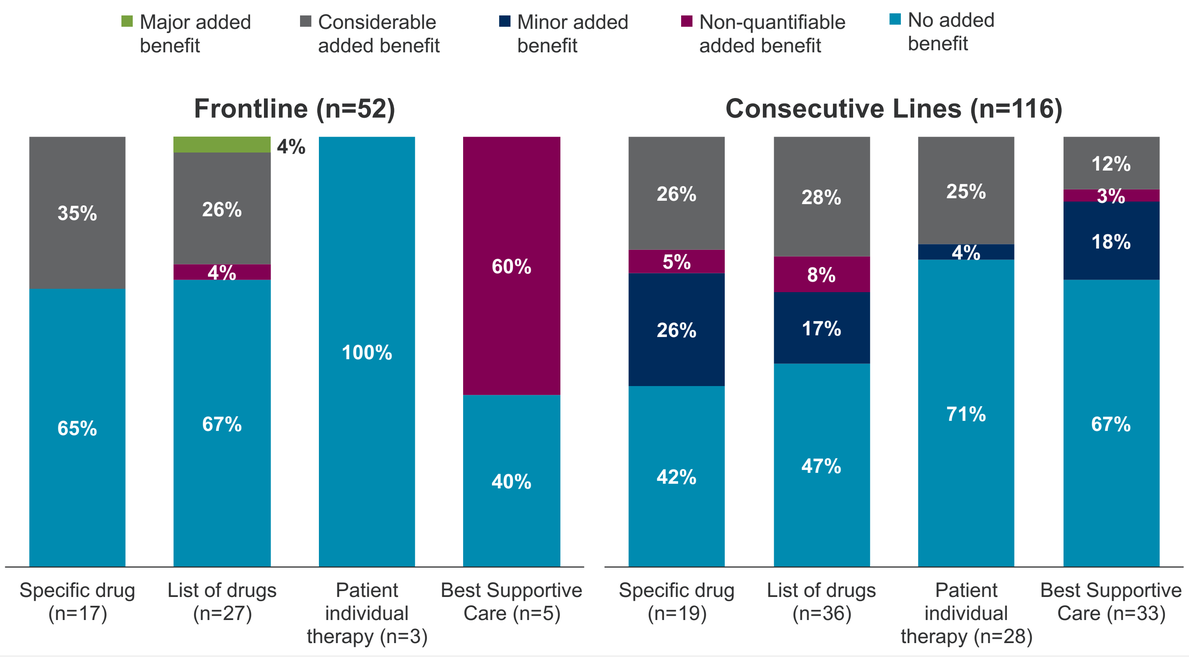
Results (cont.)

Figure 4. AMNOG Dossiers in Frontline Therapy Settings Less Often Achieved an Added Medical Benefit



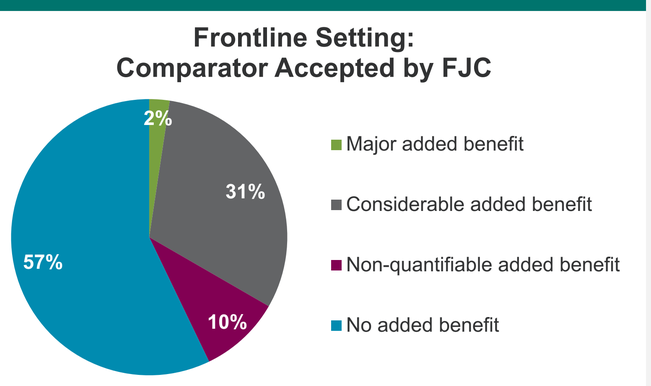
- Overall, an added medical benefit was achieved more often in consecutive therapy lines (42%) than in frontline therapy settings (35%) (**Figure 4**).
- However, the highest benefit rating (major added benefit) was only achieved in frontline therapy settings. None of the AMNOG dossiers in consecutive therapy lines achieved a major added benefit (**Figure 4**).

Figure 5. The Most Promising Appropriate Comparator Depends Largely upon the Therapy Line



- In AMNOG dossiers of frontline therapies, the appropriate comparator category BSC was linked to the highest probability to gain an added medical benefit (60%) (**Figure 5**). It should be noted that in the frontline setting, BSC has only been assigned in small populations with special disease characteristics. Hence, the choice of BSC as the appropriate comparator can be interpreted as an indicator of high unmet medical need in those settings.
- In frontline therapy settings, a major added benefit was only achieved if the appropriate comparator was a list of drugs, whereas in consecutive lines, no assessment resulted in a major added benefit (**Figure 5**).
- In consecutive therapy settings, a specific drug and a list of drugs had similar promise in the achievement of an added benefit (**Figure 5**).
- The chance to achieve a considerable added benefit was lowest for BSC (12%), but almost evenly distributed for the other three categories (specific drug, 26%; list of drugs, 28%; patient individual therapy, 25%) (**Figure 5**).
- The majority of the assessments (57%) in frontline settings did not receive an added benefit although the study comparator matched the FJC-assigned appropriate comparator (**Figure 6**).
- If the comparator used in the relevant trials did not match the appropriate comparator defined by the FJC, it was impossible to achieve an added benefit (data not shown).

Figure 6. Acceptance of the Appropriate Comparator by FJC is No Guarantee for an Added Medical Benefit



Conclusions

- In the field of oncology, a list of drugs, from which the pharmaceutical company can freely choose one specific drug, became the most commonly assigned appropriate comparator since the enactment of AMNOG, independent of the therapy line.
- A specific drug played a major role as the appropriate comparator in the first years of AMNOG benefit assessments. In 2016, the pattern changed and a list of drugs became the most prominent category of appropriate comparator. This may reflect the dramatically broadened therapeutic landscape in the field of oncology, especially with respect to drugs approved for frontline treatments.
- As of now, benefit assessments in frontline therapy settings less often resulted in an added medical benefit, even if the study comparator matched the FJC-assigned appropriate comparator.
- To provide comparative evidence against the appropriate comparator, defined by the FJC, is no guarantee for an added medical benefit, implicating that other factors play a decisive role in the AMNOG benefit assessment for frontline therapies in oncology. Most importantly, the patient relevance of study endpoints, as well as accordance of study population with label population, do have a huge impact on the benefit assessment.

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