



MARS Webinar: 10 years AMNOG – What have we learnt for drug development and pricing?

25th March 2021

Dr. Stefan Walzer

Lutz Vollmer

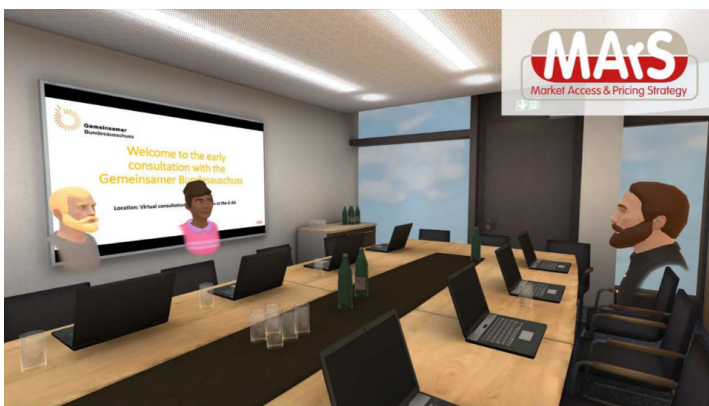
MARS Market Access & Pricing Strategy GmbH, Germany

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THE German-speaking market access experts - Austria, Germany, Switzerland





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Virtual Reality Negotiation Training Increases Negotiation Knowledge and Skill

Joost Broekens¹, Maaïke Harbers¹, Willem-Paul Brinkman¹,
 Catholijn M. Jonker¹, Karel Van den Bosch², and John-Jules Meyer²

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Broekens J., et al. (2012) Virtual Reality Negotiation Training Increases Negotiation Knowledge and Skill. In: Nakano Y., et al. (eds) Intelligent Virtual Agents. IVA 2012. Lecture Notes in Computer Science, vol 7502. Springer, Berlin, Heidelberg

Questions welcome!



- Feel free to ask questions. After the presentation, we will have time for your questions.
- Use either the Zoom chat function or the Q&A function to raise your questions or comments.
- As always, slides will be provided afterwards, and the video will be published on our website.



Upcoming Webinar

10 years AMNOG
what have we learnt for drug development and pricing?



Dr. Stefan Walzer
Speaker



Lutz Vollmer
Moderator



Prof. Dr. Thomas Hammerschmidt
University of Applied Sciences Rosenheim

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25.03.2021
9pm CET /
12am PT

10 years AMNOG – what have we learnt for drug development and pricing?

25. March 2021 21:00



Stefan Dr. Walzer
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Previous Webinars

Early paid access for drugs. Market Access to Switzerland Später ans... Teilen

The alps, cheese, banks - and early paid access for drugs! Wonderland Switzerland!

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Digital health in Germany - start of a rocket or just a big bluff?

The end of Covid-19 due to vaccines?
By when do we have our lives back?

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Our presenters and discussants today



Dr. Stefan Walzer
Speaker



Lutz Vollmer
Moderator



Prof. Dr. Thomas Hammerschmidt
University of Applied Sciences Rosenheim



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Overall – around 500 assessments until 2021

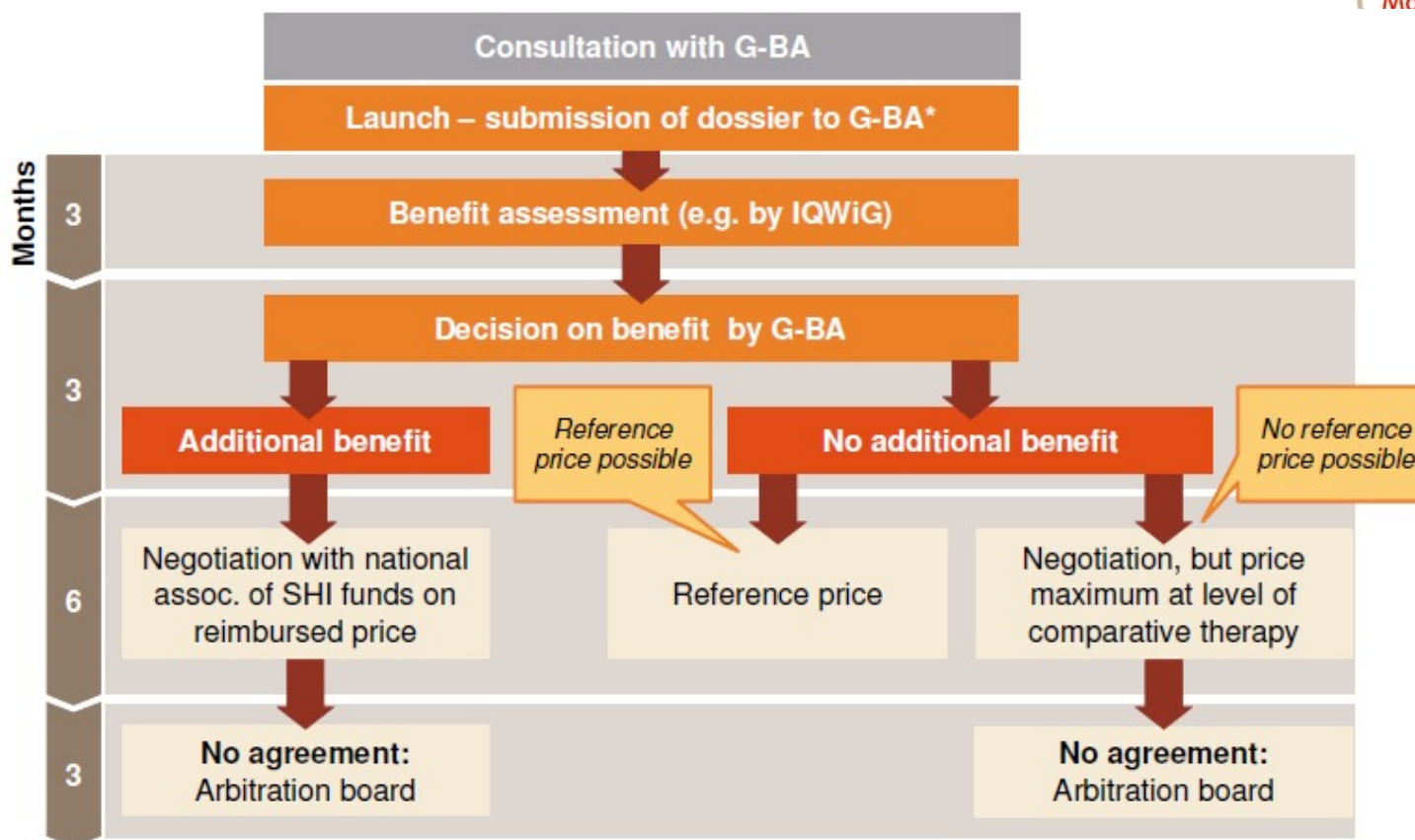


Time horizon	2011 - 2018	2011-2019
Benefit assessments		
Assessed ingredients	224	265
Finalized assessments	349	439
Re-assessments	35%	39%
Assessments without dossier	5%	5%
Orphan drugs	20%	24%
Assessments incl. subpopulations	48%	50%
Avg. Number of defined subpopulations	3.1	3.1



Until March 2021 > 500 assessments

How does the AMNOG process look like?



*G-BA Gemeinsamer Bundesausschuss – Federal joint committee

Aim: Establish Evidence for Added Benefit Rating



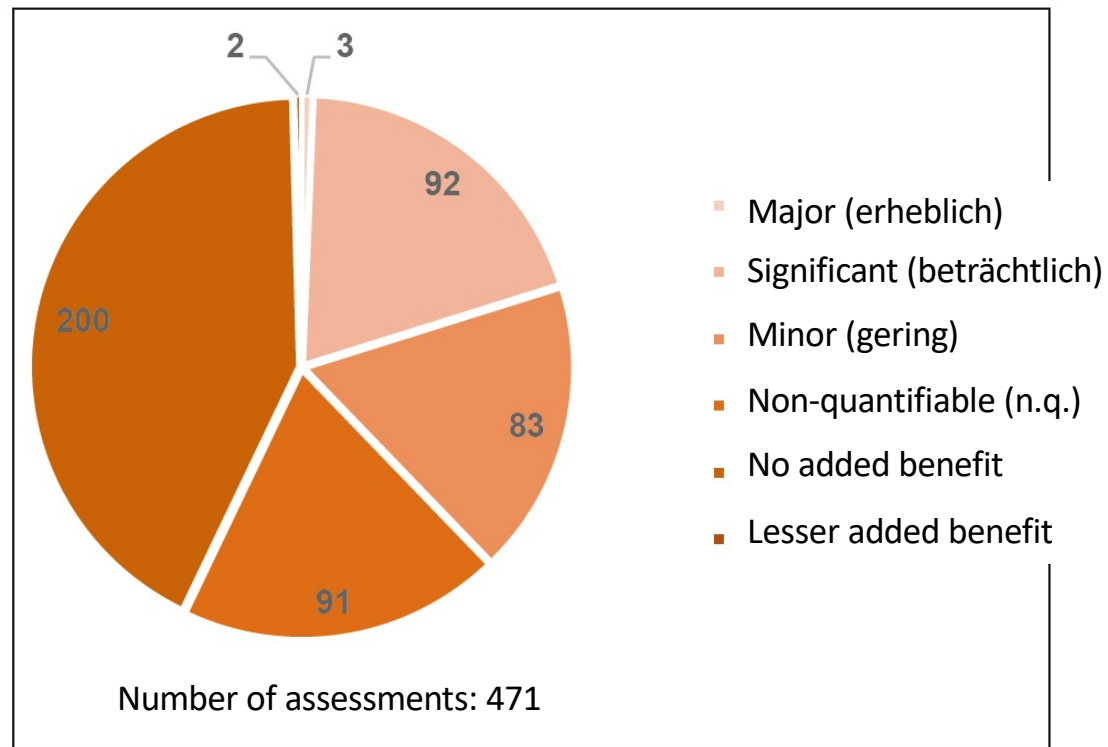
Note / Score	Decision Category	Definition	Price negotiation	Implication for pricing	EU prices considered
1	Significant or Major added benefit (erheblich)	Sustainable and not yet achieved significant improvement of the relevant therapeutic benefit	Yes	Adjusted premium vs. the appropriate comparator therapy in pricing negotiation. Important: Potential price anchors (other therapies) could be discussed. Key negotiation driver is especially the certainty on the added benefit.	Yes
2	Considerable added benefit (beträchtlich)	Not yet achieved considerable improvement of the relevant therapeutic benefit	Yes		Yes
3	Minor/Marginal added benefit (gering)	Not yet achieved moderate and not only marginal improvement of the relevant therapeutic benefit	Yes		Yes
4	Non-quantifiable added benefit (nicht quantifizierbar)	Added benefit exists, but the scientific data basis does not allow for quantification	Yes		Yes
5	No added benefit		No, if a product can be put into a reference price group	Reference price or as a maximum the price of the appropriate comparator	No
6	Lesser benefit (geringerer Nutzen)	Benefit is lower than the appropriate comparator	No	Discount on the appropriate comparator	No

Added benefit granted for orphan drugs



Note / Score	Decision Category	Definition	Price negotiation	Implication for pricing	EU prices considered
1	Significant or Major added benefit (erheblich)	Sustainable and not yet achieved significant improvement of the relevant therapeutic benefit	Yes	Adjusted premium vs. the appropriate comparator therapy in pricing negotiation. Important: Potential price anchors (other therapies) could be discussed. Key negotiation driver is especially the certainty on the added benefit.	Yes
2	Considerable added benefit (beträchtlich)	Not yet achieved considerable improvement of the relevant therapeutic benefit	Yes		Yes
3	Minor/Marginal added benefit (gering)	Not yet achieved moderate and not only marginal improvement of the relevant therapeutic benefit	Yes		Yes
4	Non-quantifiable added benefit (nicht quantifizierbar)	Added benefit exists, but the scientific data basis does not allow for quantification	Yes		Yes
5	For Orphan Drugs there are only four potential additional benefit levels!				
6					

57% of assessments received an added benefit



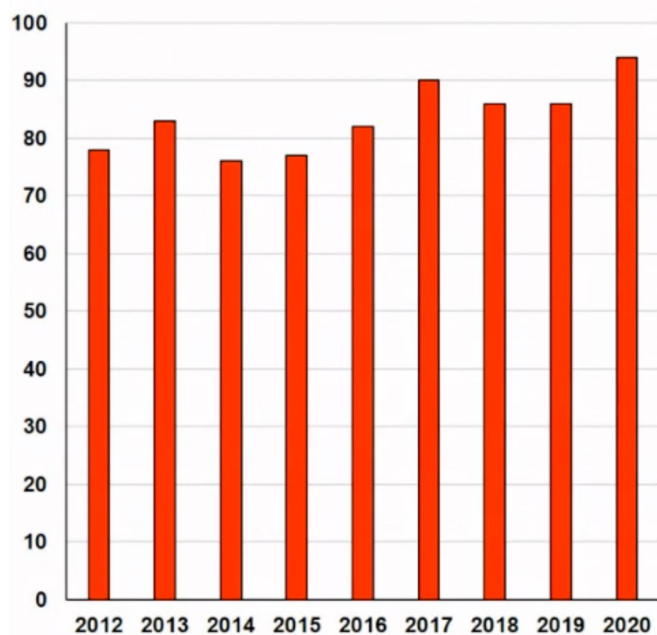
G-BA oral hearing – important event



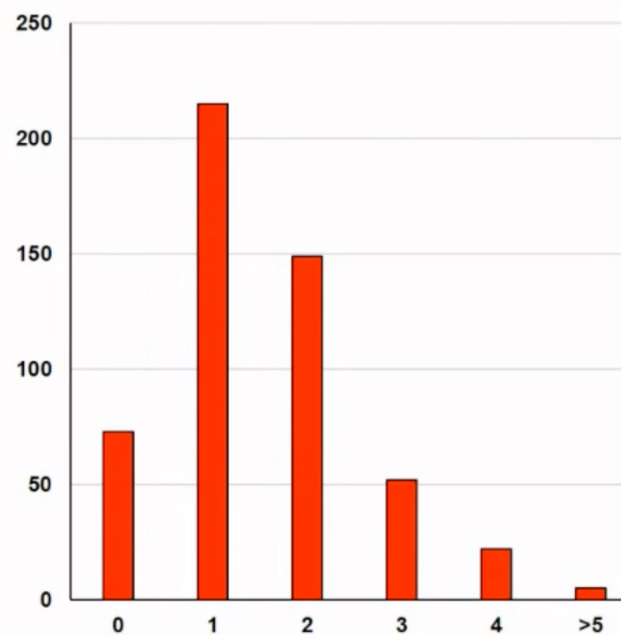
Participation of KOLs, ideally medical association important



Number of assessments with medical associations



Number of involved medical associations



Heterogeneity in 1/3 of all assessments between IQWiG and G-BA



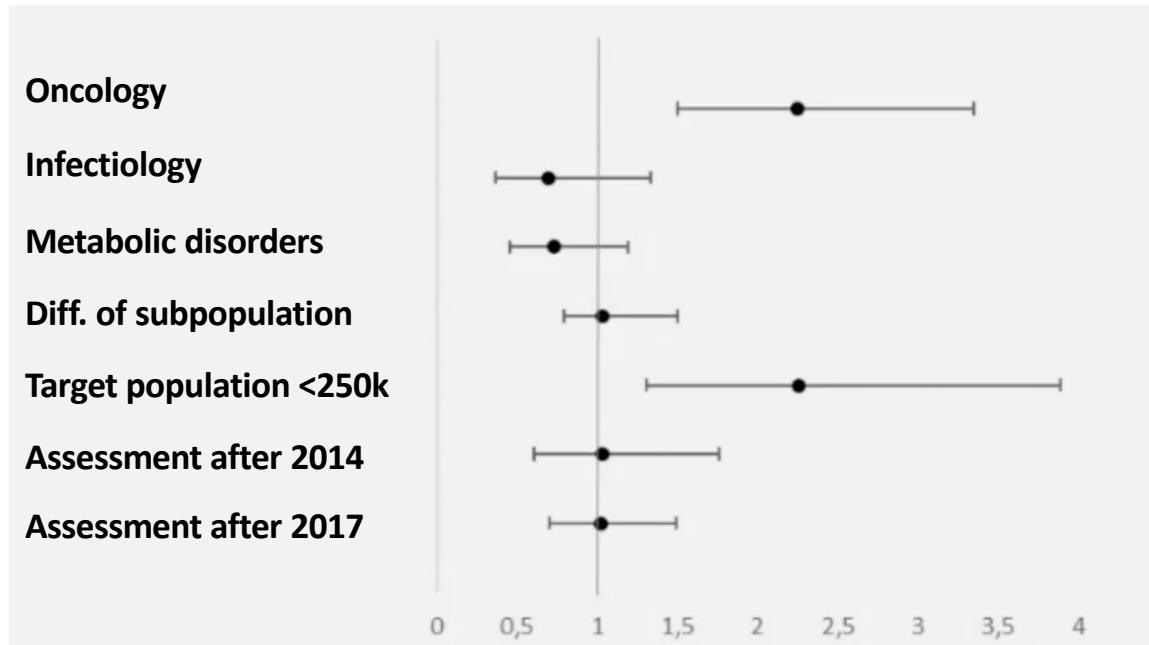
Note / Score	Significant or Major added benefit (erheblich)	Considerable added benefit (beträchtlich)	Minor/Marginal added benefit (gering)	Non-quantifiable added benefit (nicht quantifizierbar)	No added benefit	Lesser benefit (geringerer Nutzen)
Significant or Major added benefit (erheblich)	2	22	2	1	0	0
Considerable added benefit (beträchtlich)	0	35	17	1	3	0
Minor/Marginal added benefit (gering)	0	7	20	0	4	0
Non-quantifiable added benefit (nicht quantifizierbar)	0	10	4	13	3	0
No added benefit	0	5	20	13	176	0
Lesser benefit (geringerer Nutzen)	0	0	0	0	7	1

Zusatznutzen: IQWiG = G-BA	N = 247 (67%)
Zusatznutzen: IQWiG > G-BA	N = 53 (14%)
Zusatznutzen: IQWiG < G-BA	N = 66 (18%)



What have we learnt for drug development?

Various impact factors for the likelihood of an added benefit



Odds ratio with 95% confidence interval
(1= no effect; <1 drug has higher chance of added benefit)

What are the needs of payers?

Patientenrelevante Endpunkte sind:

- **Mortalität**
- **Morbidität**, bei der vorliegenden Indikation insbesondere:
 - o Motorische Symptome (z.B. Paresen, Steifheit)
 - o Körperliche Funktionalität (z.B. unabhängiges Sitzen, Stehen, Gehen, Feinmotorik, Nahrungsaufnahme)
 - o Schmerzen
 - o Fatigue
- **(gesundheitsbezogene) Lebensqualität**
 - o Die Verwendung sowohl eines krankheitsspezifischen als auch eines generischen Fragebogens zur Lebensqualität (bevorzugt SF-36) wird empfohlen. Die Validität der mit dem iNQoL (Individual Neuromuscular Quality of Life questionnaire) erhobenen Ergebnisse ist im Dossier darzustellen.
 - o Die Messung der Lebensqualität sollte zumindest zu Beginn und zum Ende der Behandlungszeit erfolgen, möglichst auch zusätzlich zum Ende der Nachbeobachtungszeit.

- 4 -



- o Die Erhebung der krankheitsspezifischen Lebensqualität wird ausdrücklich befürwortet und sollte mit geeigneten, indikationsspezifisch validierten Messinstrumenten erfolgen.
- o Um die Aussagekraft von Daten zur Lebensqualität und Morbidität zu erhöhen, wird empfohlen, diese über das Therapieende mit der Prüflintervention hinaus zu erheben. Dies gilt insbesondere für Behandlungssituationen, in denen das Therapieende oder ein Therapiewechsel mit Auswirkungen auf die Lebensqualität und Morbidität assoziiert wird.

- Nebenwirkungen

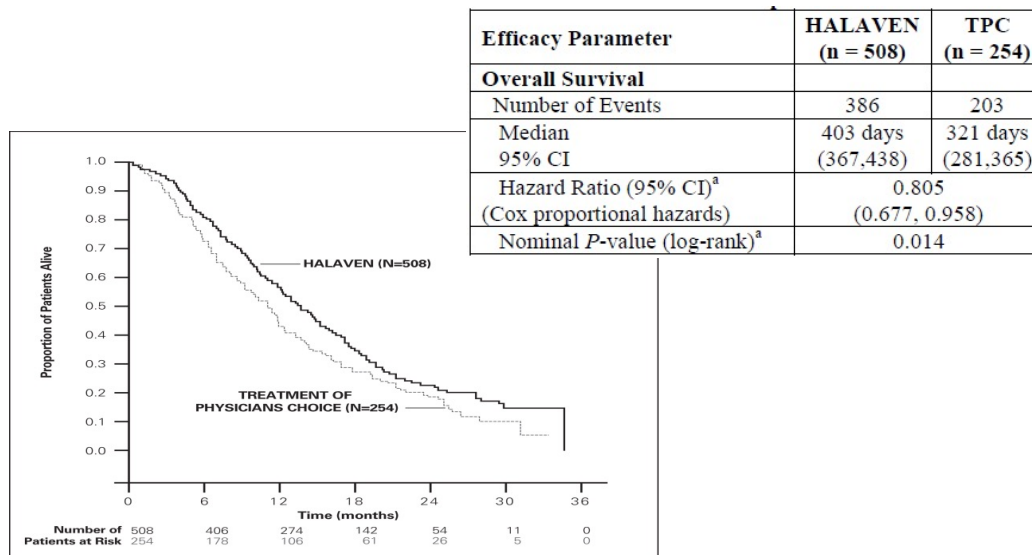
Es sind unerwünschte und schwerwiegende unerwünschte Ereignisse (UE und SUE) darzustellen: sowohl als Gesamtraten als auch jeweils differenziert nach Krankheitskonzepten/Organsystemen (als SOCs¹ und PT² nach MedDRA³ und für spezifische UE zusätzlich, sofern möglich, als SMQs⁴) sowie nach Schweregrad (CTCAE⁵ und/oder eine andere etablierte bzw. validierte indikationsspezifische Klassifikation). Therapieabbrüche aufgrund von UE sind ebenfalls darzustellen.

- Mortality
- Morbidity
 - Symptoms
 - Physical functioning
 - Pain
 - Fatigue
 - ...
- HRQoL
 - Validated disease specific questionnaire
 - Generic questionnaire (EQ-5D)
- Adverse events

NO PFS ?!

So, overall survival is the core?

Experience – Eribulin (initial assessment) benefit only for subgroup



• GBA decision:

- The GBA was following the IQWiG recommendations
- A minor additional benefit was ascertained for the subpopulation that is not eligible for further anthracycline or a taxane based therapy
- **For all other patients no additional benefit was ascertained**

General study design standards



- Study duration with at least 6 months acceptable (better: 1 year)
- Randomization method accepted by the G-BA (IWRS; permuted blocks)
- Two confirmatory RCTs could grant the highest evidence level within the assessment framework (with correct endpoints, comparator, ...)
- Multiplicity testing rule acceptable...
 - ... however: individual significance level always needed independent of rule applied
- Choice of „right“ stratification factor
- Choice of correct country specific comparator
 - e.g. Best Supportive Care is not always Best Supportive Care

Adverse Event specifications



- Safety data coded using MedDRA term
- The following AE analyses are for example always required by the German G-BA:
 - AEs
 - AEs of special interest
 - SAEs
 - Treatment emergent AEs
 - Discontinuations

Minimum statistical requirements



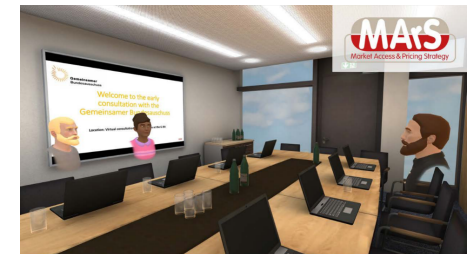
- For all endpoints to be submitted to the G-BA the following statistics need to be calculated (if applicable):
 - Arithmetic mean, 95% Confidence interval, standard deviation
 - Relative Risk, Odds Ratio, Risk Difference, Hazard Ratio
 - Hedges' g (effect size measure)

- Level of significance would always need to be calculated

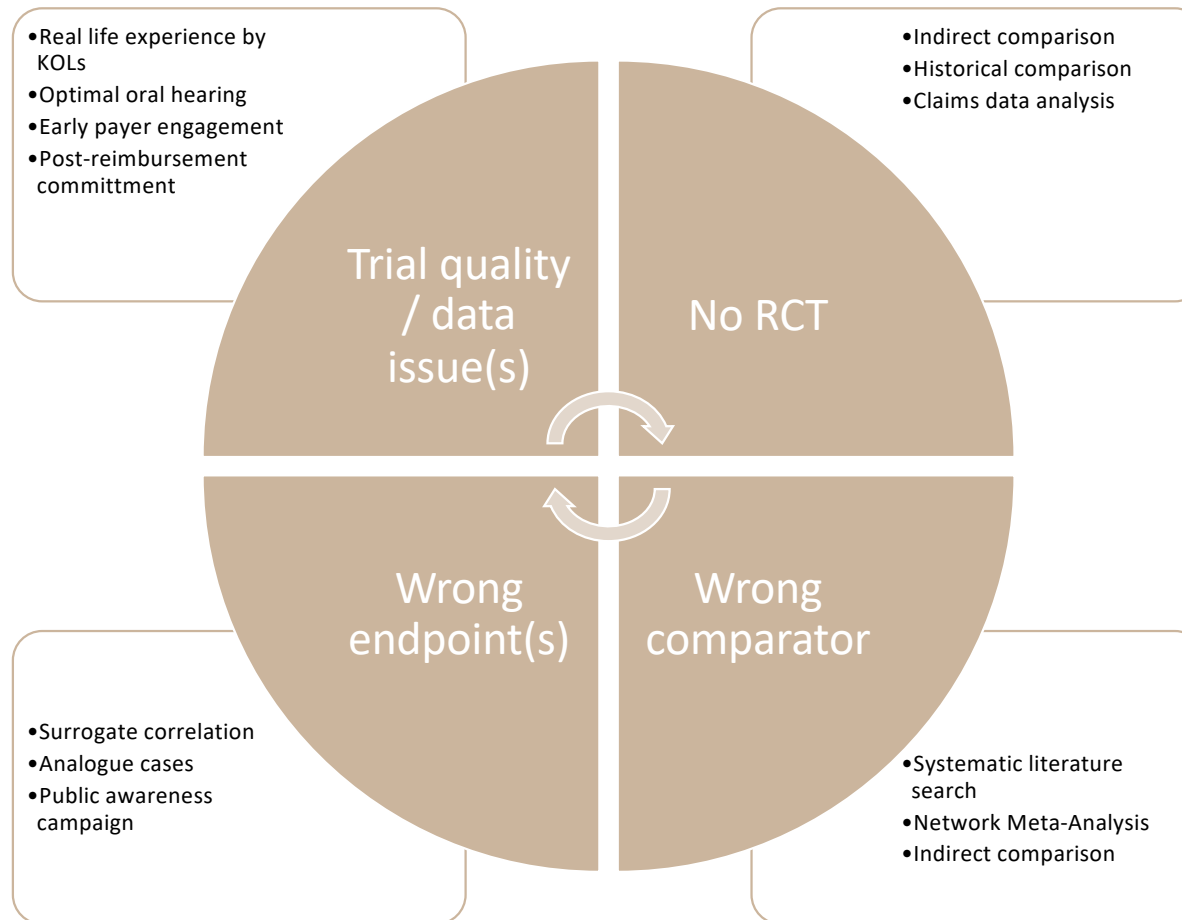
Planning as most important



- Early G-BA engagement of utmost importance in order to optimize commercial success
- Consultation should start around clinical phase II – payer involvement in the planning of phase III package indispensable
- In case of non-optimal clinical package early risk minimization tactics required



How to optimize a G-BA dossier?





What have we learnt for drug's pricing?

... and after the benefit assessment?



The price negotiation



- GKV-SV Berlin
- Negotiation room
- Preparation room

Pre- and post-Covid-19

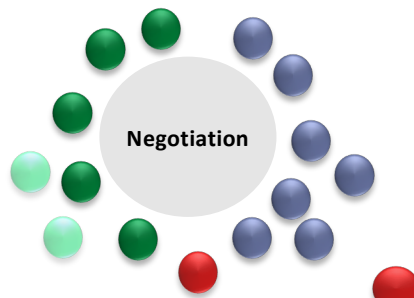
Since Covid-19 pandemic

- Web-conferences
- Negotiation team communication (messenger, meetings, separate telephone line, ...)

Structure of the negotiation process at the GKV-SV



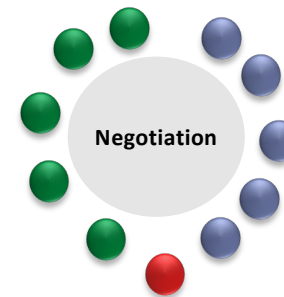
- Two further meetings planned, between first and last meeting
- Upon agreement of parties another meeting is possible
- Last meeting max. 3 weeks prior to price publication



- First meeting within 4 weeks after GBA decision
- 5 participants per party
- 2 in addition are allowed upon agreement.



Guest of the national association of private health insurances



Private health insurance has to be informed within 5 working days after last negotiation date about rebate / reimbursement price.

Publication in official price list: Lauer Taxe

Basket of European reference price countries for price negotiation



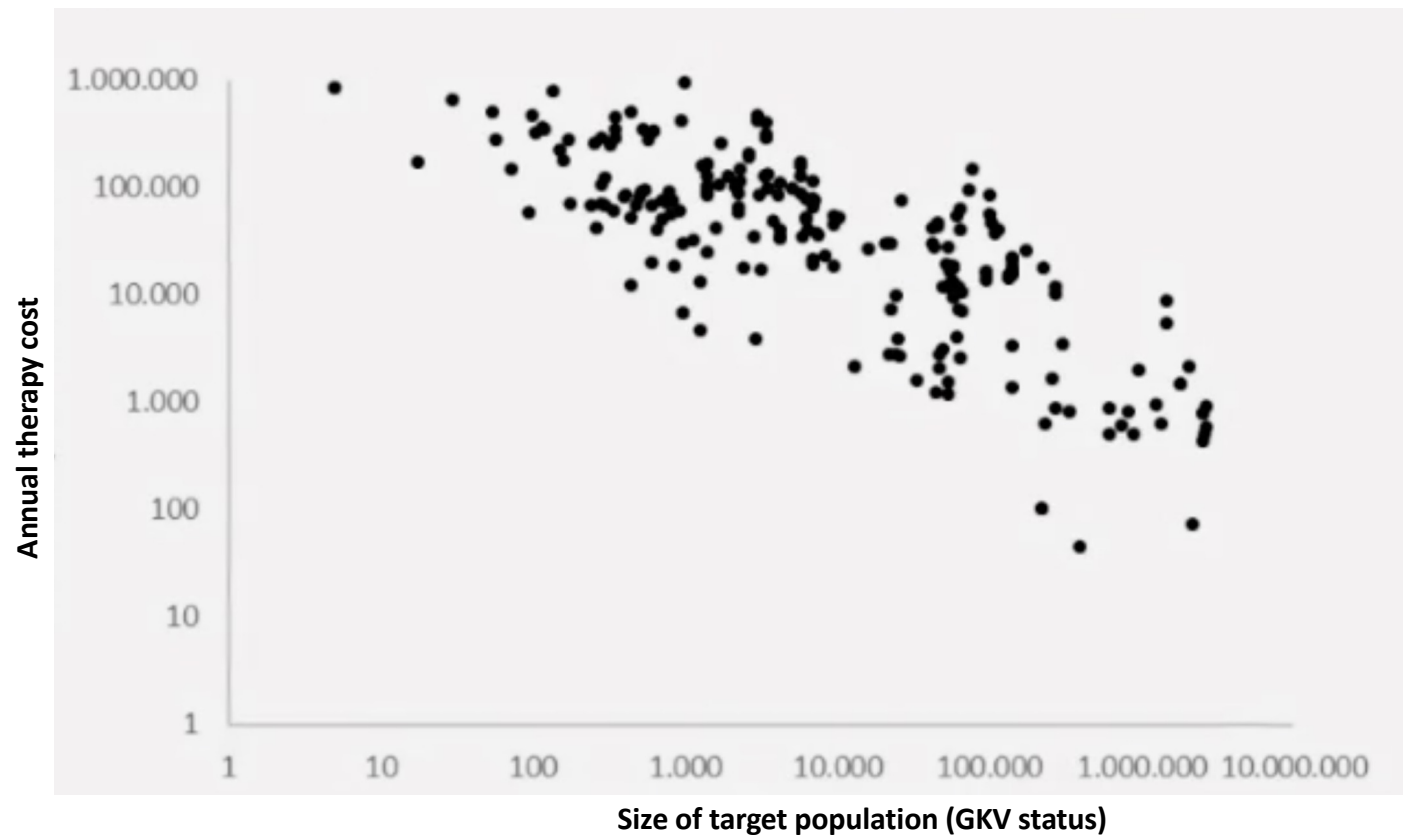
1. Austria
2. Belgium
3. Czech Republic
4. Denmark
5. Finland
6. France
7. Greece
8. Ireland
9. Italy
10. Portugal
11. Sweden
12. Spain
13. Slovakia
14. Spain
15. UK



Drivers in the price negotiations with the GKV-SV



Correlation between size of target population and the negotiated annual therapy cost



Price impact foreseeable?

RESEARCH

Open Access



Benefit assessment in Germany: implications for price discounts

Ulrike Theidel^{1*} and J-Matthias Graf von der Schulenburg²

Overall

Size of target population	<i>n</i>	Mean	Min	Max	SD
0-< 1000	34	20.84	1.00	53.71	12.15
1000-< 2500	38	21.28	0.00	42.54	11.53
2500-< 7500	31	19.79	4.74	39.44	9.00
7500-< 25000	32	21.61	2.01	46.44	11.43
25000-< 150000	34	23.88	3.16	67.30	15.12
150000+	24	25.18	2.01	78.02	19.50

Orphan drugs

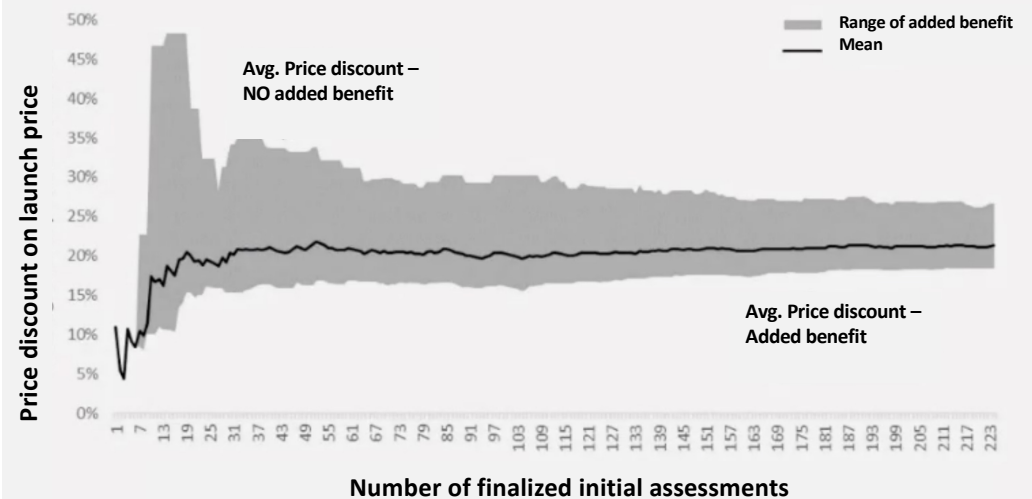
Size of target population	<i>n</i>	Mean	Min	Max	SD
0-< 300	10	13.70	1.00	24.50	8.15
300-< 1500	10	20.66	9.00	29.78	6.52
1500+	9	20.81	10.96	25.54	4.66

All discounts presented in %

Abbreviations: *Min* minimum, *Max* maximum, *SD* standard deviation

Source: Theidel U. Health Economics Review. 2016

Development of price discounts according to §130b SGB V

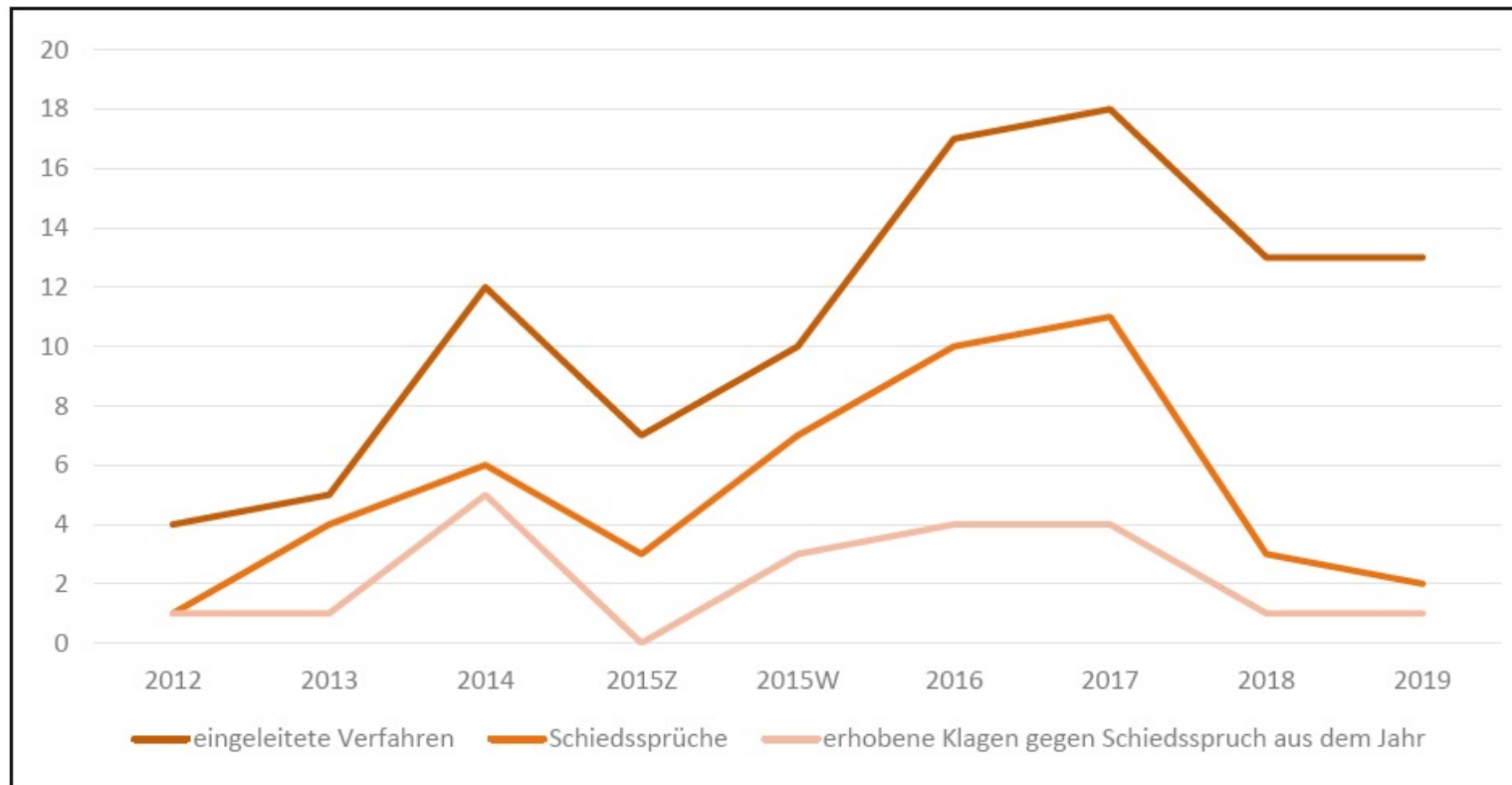


AMNOG report 2020 - <https://www.dak.de/dak/download/report-2335144.pdf>

Arbitration decisions as a balance of interests - rate of claim as a yardstick for acceptance of the decision?



Decreasing numbers of cases since 2018





10 years AMNOG
what have we learnt for drug development and pricing?

Prof. Dr. Thomas Hammerschmidt
Technical University of Applied Sciences
Rosenheim

Outline

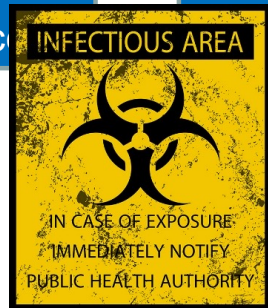


- ◆ A brief history of ...
- ◆ Key success factors
- ◆ Guidance for clinical development
- ◆ Correlation of benefit assessment and price negotiations and drivers
- ◆ Future of AMNOG

A brief history of ...



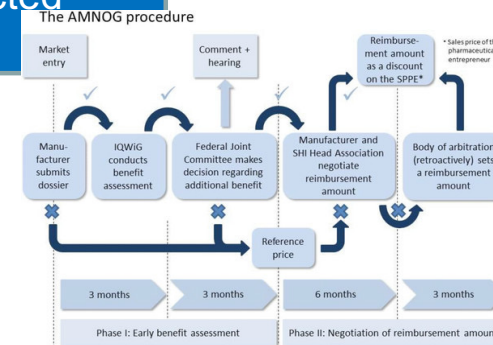
1970s-1990s:
Ideas: market access, HTA, value-based pricing
Host: Science



1990s-2010s:
A new host:
Health system decision makers



2011:
Germany became infected

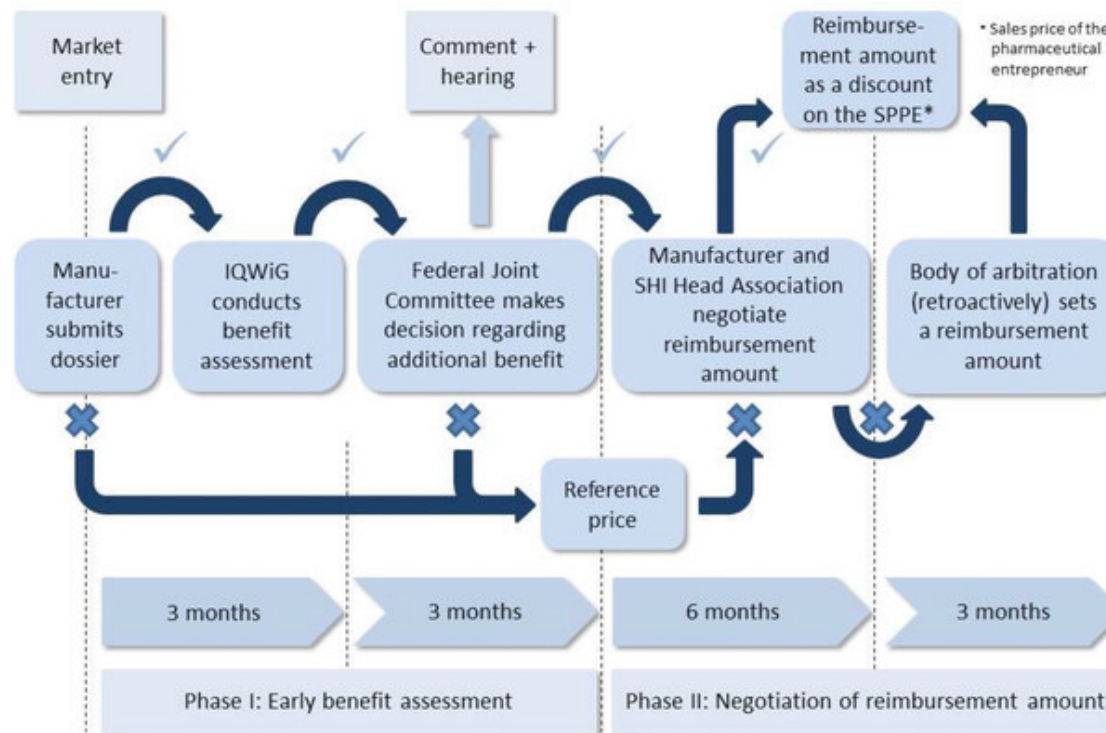


Images: <https://www.marketingweek.com/new-normal-trends-before-covid/>, <https://www.onlinenursingdegrees.org/types/infectious-disease.htm>, <https://newdaychurch.cc/series/pandemic/>, <https://weknowyourdreams.com/paradise.html>, <https://www.researchgate.net/publication/281483062> Implementation of AMNOG An industry perspective/figures?lo=1

Today: 10 years of AMNOG

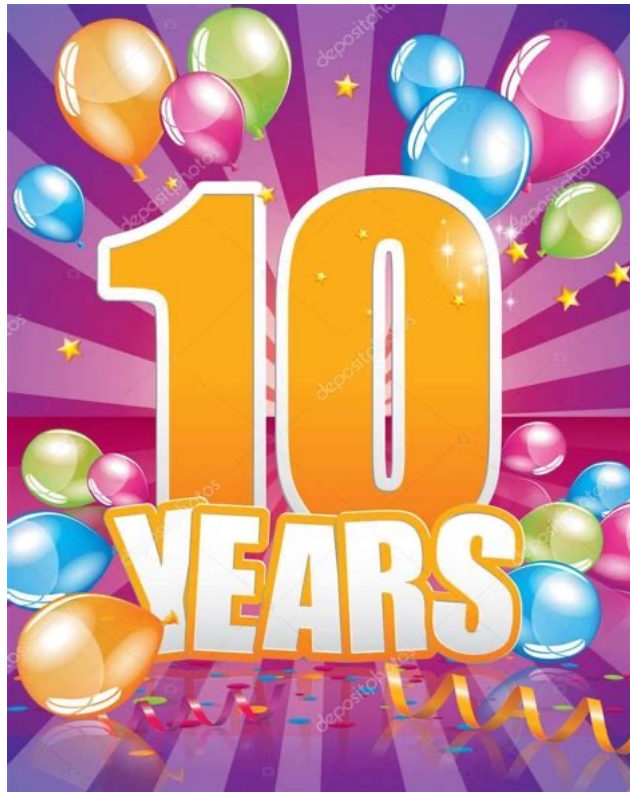


The AMNOG procedure



Images: <https://www.marketingweek.com/new-normal-trends-before-covid/>,
https://www.researchgate.net/publication/281483062_Implementation_of_AMNOG_An_industry_perspective/figures?lo=1

Today: 10 years of AMNOG



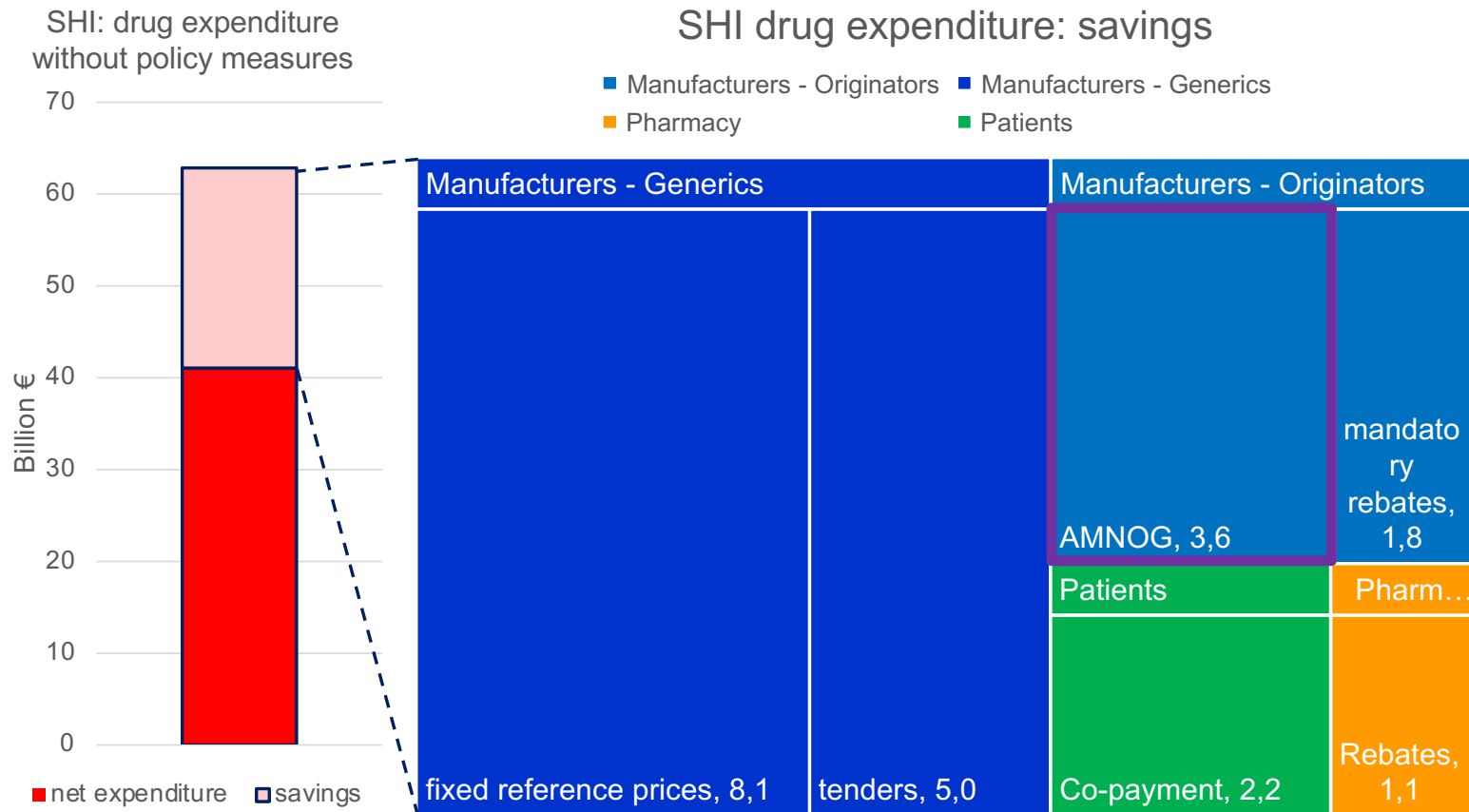
Images: <https://www.marketingweek.com/new-normal-trends-before-covid/>,
https://www.researchgate.net/publication/281483062_Implementation_of_AMNOG_An_industry_perspective/figures?lo=1

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Images: <https://www.marketingweek.com/new-normal-trends-before-covid/>,
https://www.researchgate.net/publication/281483062_Implementation_of_AMNOG_An_industry_perspective/figures?lo=1

Relevance of AMNOG



Key success factors



- ◆ Informal aspects → the “how“



- ◆ Formal aspects → the “what“



Clinical development

Images: <https://www.salesforce.com/>, <https://www.dreamstime.com/stock-photo-customers-needs-concept-marketing-specialist-think-customer-represented-text-written-virtual-board-image54728750>, <https://energyconsumersofthecarolinas.org/transparency-is-the-new-objectivity/>, <https://www.joegirard.com/posts/sincerity/>, <https://qualityinspection.org/manufacturing-process-control-china/>, <https://medone-cro.com/services/>

Guidance for clinical development



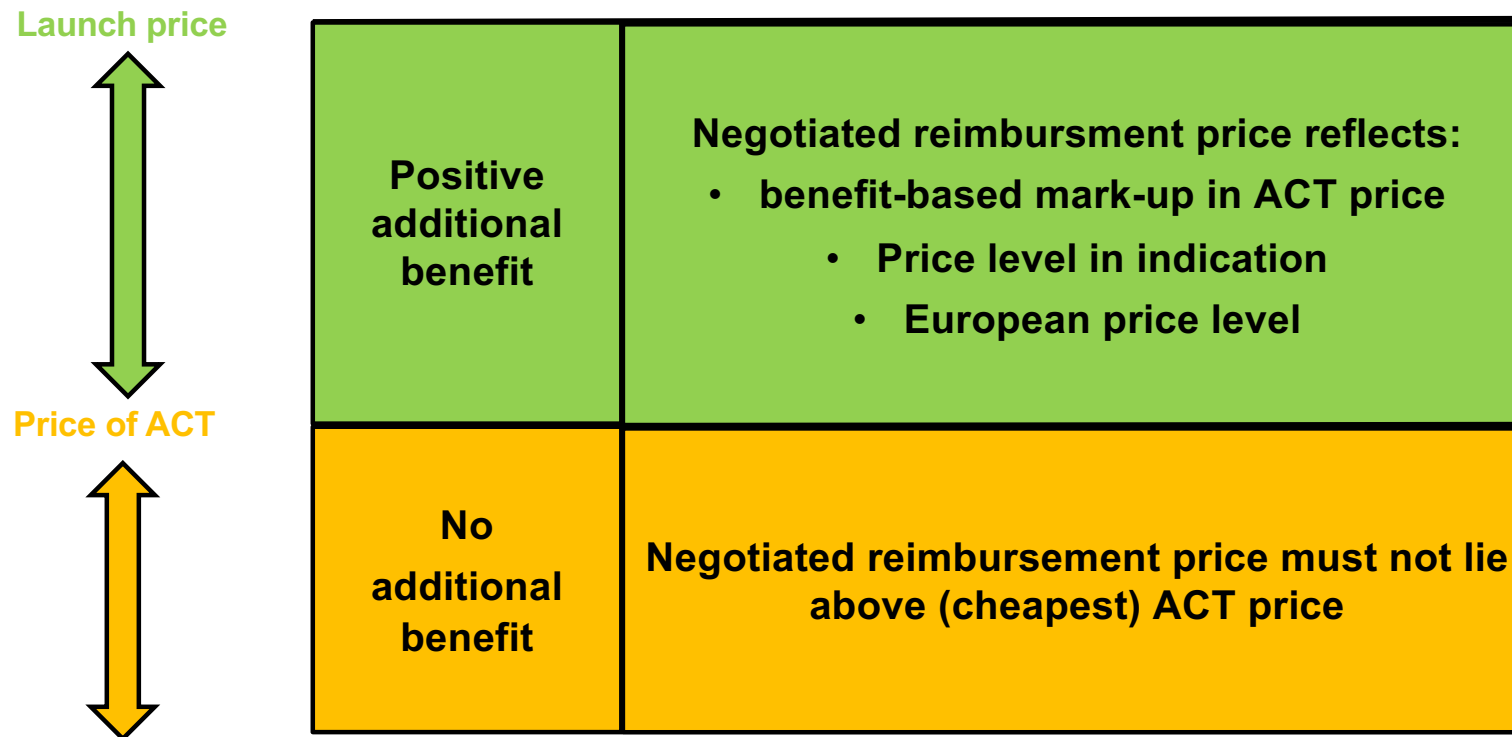
Clinical development



- ◆ Appropriate comparator therapy (ACT) is defined by the G-BA
 - Direct H2H
 - Indirect comparisons
 - Missing comparative data
- ◆ Patient relevant endpoints defined by law
 - Mortality
 - Symptoms
 - Health-related quality of life
 - Side-effects
 - Surrogate endpoints (lab parameters or imaging)

Images: <http://metamorphoseindia.com/career-guidance/>, <https://medone-cro.com/services/>

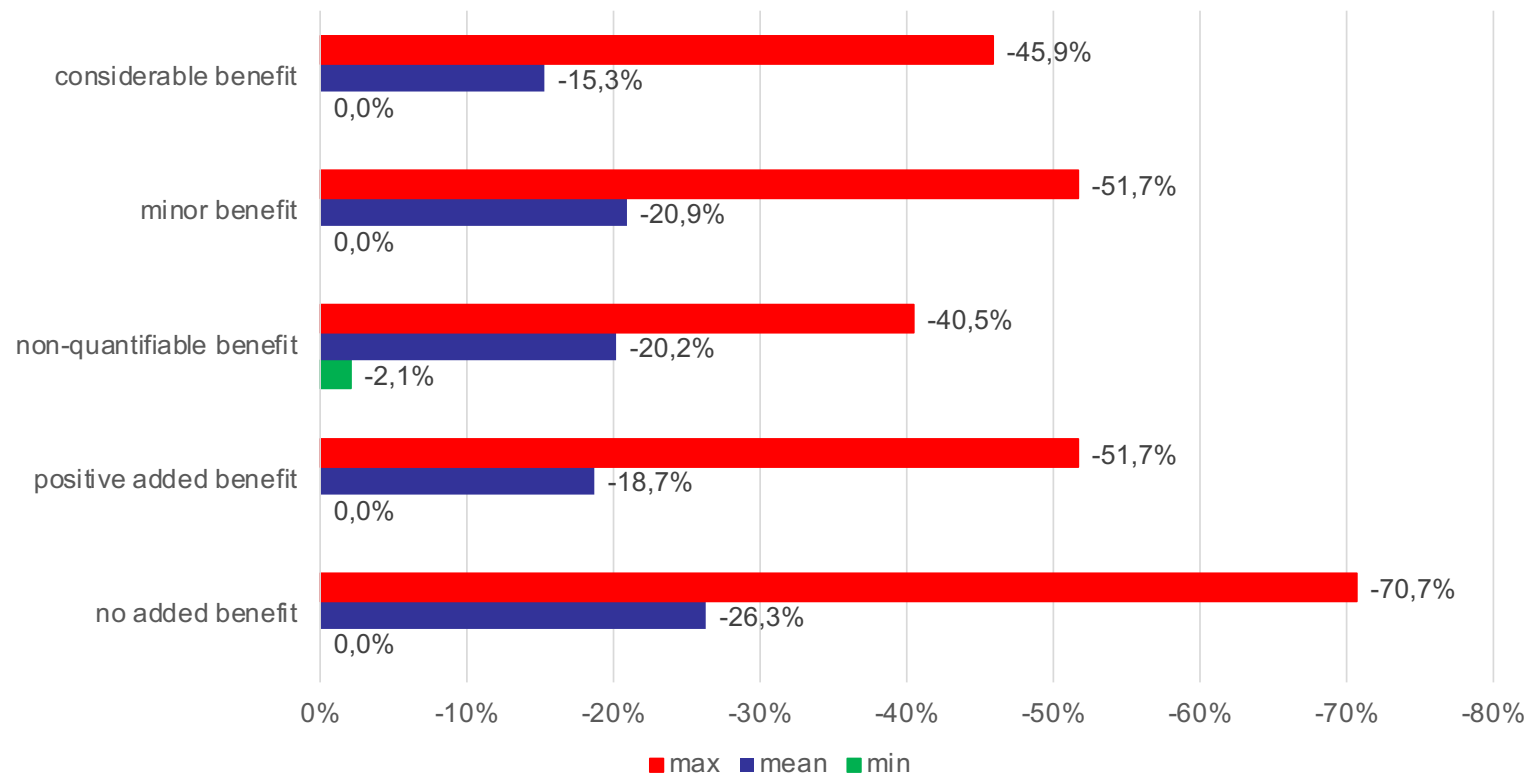
The reimbursement price negotiation



Correlation of benefit assessment and negotiated price

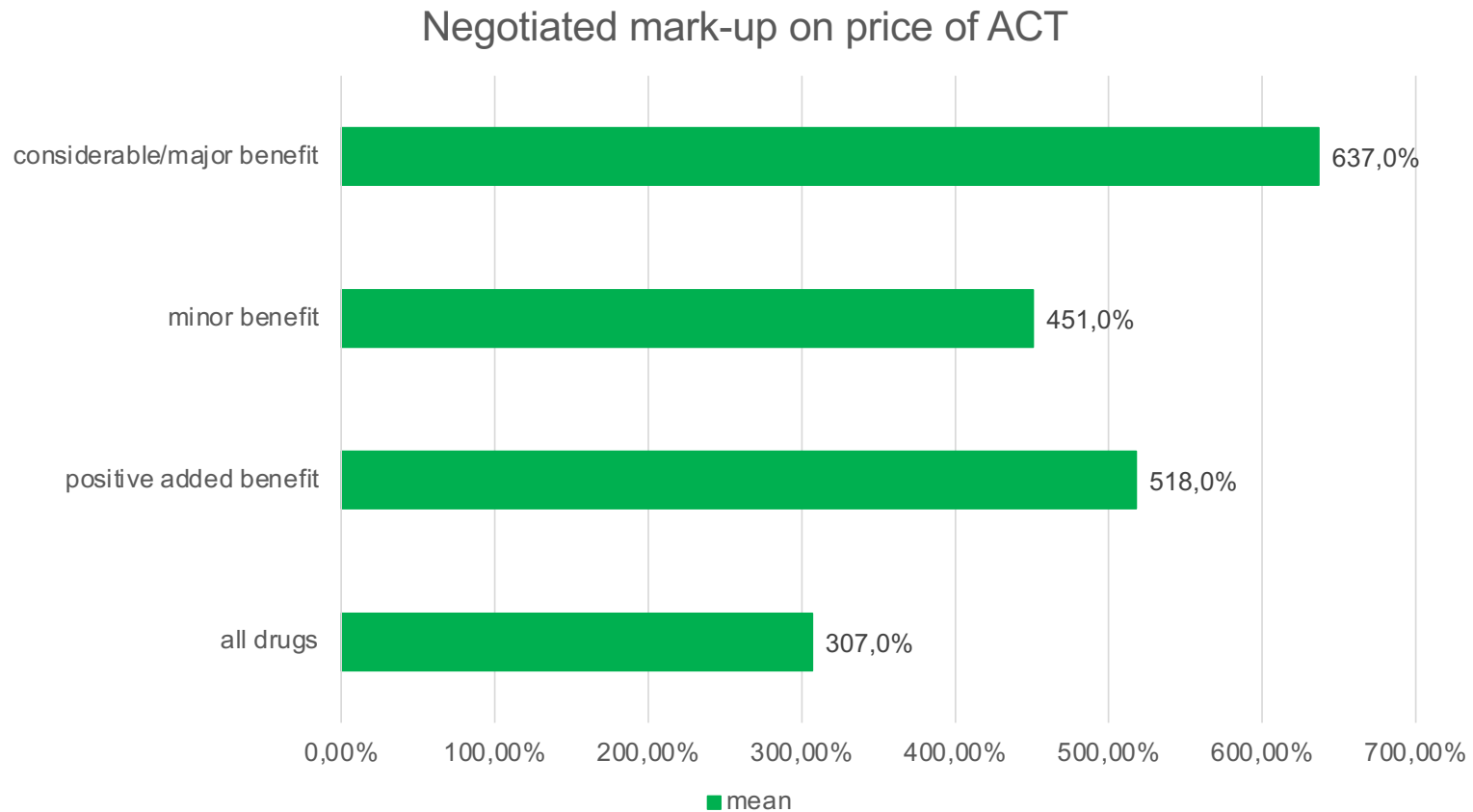


Negotiated rebates (vs. Launch price)



Source: AMNOG Report 2020, Tab. 24

Correlation of benefit assessment and negotiated price



Source: AMNOG Report 2020, p 231-232

Scenarios for the reimbursement price negotiation (company perspective)



Positive additional benefit



No additional benefit

ACT patent-protected



ACT generic



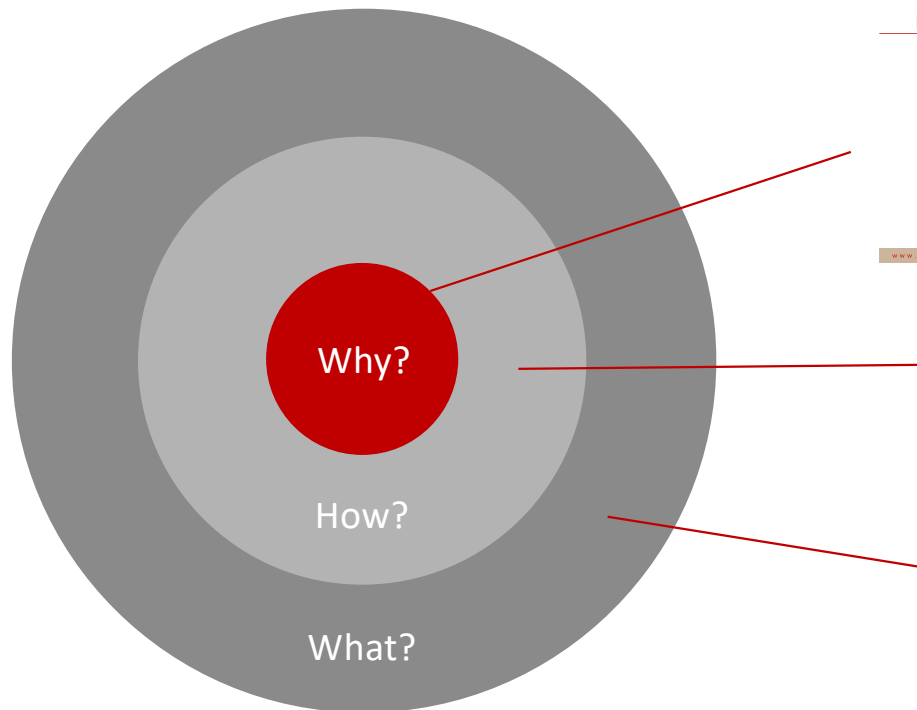


- ◆ A learning system that has to and will evolve
- ◆ No compromise on clinical data
- ◆ Limited use of real-world data, modelling studies ...
- ◆ QoL, PROs will become more relevant
- ◆ Limited use of innovative contracting
- ◆ Cost-benefit assessment?
- ◆ Free pricing during first 12 months?
- ◆ Orphan drugs “privileges“?
- ◆ European HTA?

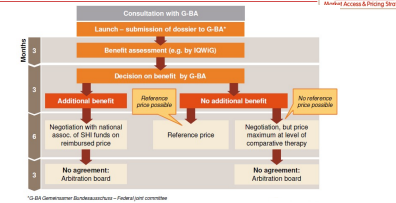
Image: <https://www.astrolantis.de/shop/magische-kristallkugel/>

Conclusions

Plan the submission properly in order to optimize price



How does the AMNOG process look like?



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Planning as most important



- Early G-BA engagement of utmost importance in order to optimize commercial success
- Consultation should start around clinical phase II – payer involvement in the planning of phase III package indispensable
- In case of non-optimal clinical package early risk minimization tactics required



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Price impact foreseeable?



Benefit assessment in Germany: implications for price discounts

Year	Min	Max	Mean
0 - 1000	34	2884	1380
1000 - 2000	38	2120	1050
2000 - 3000	31	1974	1214
3000 - 4000	32	2141	1040
4000 - 5000	34	2388	1314
5000 - 6000	24	2018	1022



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10 years AMNOG

what have we learnt for drug development and pricing?



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Pricing Strategy GmbH



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Speaker



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Moderator



Prof. Dr. Thomas Hammerschmidt
University of Applied Sciences Rosenheim

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12am PT

Time for questions ...



10 years AMNOG what have we learnt for drug development and pricing?



Market Access &
Pricing Strategy GmbH



Dr. Stefan Walzer
Speaker



Lutz Vollmer
Moderator



Prof. Dr. Thomas Hammerschmidt
University of Applied Sciences Rosenheim

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The story continuous on Clubhouse

A promotional poster for a Clubhouse event. At the top, it says '@ CLUBHOUSE' and 'recorded session'. The main title is 'MARS GOES CLUBHOUSE' in a large, curved font, with a rocket launching from the right. Below the title is a large Mars bar with the MARS logo on its wrapper. The date and time are '1.4. 20:30 Uhr'. At the bottom, it reads '10 Jahre AMNOG' and 'Einfluss auf klinische Entwicklung und Pricing von Medikamenten in Deutschland?'.

@ CLUBHOUSE
recorded session

MARS GOES CLUBHOUSE

1.4.
20:30
Uhr

10 Jahre AMNOG
Einfluss auf klinische Entwicklung und
Pricing von Medikamenten in Deutschland?



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Bibiane Schulte-Bosse
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Dr. Mathias Flume
KV Westfalen-Lippe

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Market Access &
Pricing Strategy GmbH



Dr. Stefan Walzer
Speaker



Willi Woellner
MediClin clinics Bad Wildungen



Lutz Vollmer
Moderator

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29.04.2021
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