



Global Health Economic Consulting

Health Economic Show Cases



AHEAD is specialized on market access strategy and solutions for Germany and on global health economics



AHEAD

Market Access, Pricing & Reimbursement Strategy



Reimbursement Applications & Submissions

Global Health Economic Strategy Consulting & Implementation



Global Research Dissemination & Publications

AHEAD examples for the dissemination of health economic evidence as research manuscripts, congress posters and oral presentations



Manuscripts

Mickisch GH, **Schwander B**, Escudier B, Bellmunt J, Maroto P, Porta C, Walzer S, Siebert U: [Indirect treatment comparison of bevacizumab + interferon- \$\alpha\$ -2a vs tyrosine kinase inhibitors in first-line metastatic renal cell carcinoma therapy](#); Clinicoecon Outcomes Res. 2011;3:19-27. Epub 2011 Jan 25

Schwander B, Gradl B, Zöllner Y, Lindgren P, Diener HC, Lüders S, Schrader J, Villar FA, Greiner W, Jönsson B: [Cost-utility analysis of eprosartan compared to enalapril in primary prevention and nitrendipine in secondary prevention in Europe - The Health Model](#); Value in Health 2009 Vol 12 (6): 857-870

Congress Posters

Mickisch GH, **Schwander B**, Cassinello JG, Carles J, Walzer S, Nuijten M: Simulation and Comparison of Progression-Free Survival Outcomes of Sequential Therapy in Metastatic Renal-Cell Carcinoma; ISPOR 13th Annual European Congress Prague, Czech Republic, November 2010 (PCN 23)

Schwander B, de Castro Carpeño J, Heigener D, Wright E, Bischoff HG, Walzer S: Comparative Effectiveness Assessment of Erlotinib versus Gefitinib in First-Line EGFR Activating Mutation Positive Non-Small Cell Cancer; 16th ISPOR Annual Meeting, Baltimore, MD, USA, May 2011 (PCN7)

Oral Presentations

Schwander B, Mickisch GH, Walzer S, Siebert U: Methodological issues of control arm adjustments for comparative effectiveness assessments: An example based on the comparison of first-line bevacizumab+interferon alpha-2a vs sunitinib in renal cell carcinoma; [ISPOR](#) 12th Annual European Congress, Paris, France, October 2009 (CN8)

Schwander B, Lindgren P, Gradl B: The cost-effectiveness (cost-utility) of eprosartan in hypertensive patients with cerebrovascular disease in Belgium, Germany, Spain, UK, and Sweden; ISPOR 10th European Congress, Dublin, Ireland, October 2007 (CV8) [only abstract available]

AHEAD showcases for the health economic assessments by decision analytic modeling



1. Diagnoses of obscure GI Bleeding via Capsule Endoscopy

- Decision tree model developed in TreeAge - setting Germany (Europe)
- Capsule endoscopy vs. push enteroscopy

2. Sequential Therapy in Renal Cell Carcinoma

- Markov model programmed in TreeAge and MS Excel
- Simulation of the clinical outcomes of several therapy sequences

3. Antihypertensive Therapy – Primary & Secondary Prevention

- Markov model programmed in Delphi and C++ – setting Germany (Europe)
- Eprosartan vs. elanapril and vs. nitrendipine

4. Therapy in EGFR Mut+ Non-Small Cell Lung Cancer

- Markov model programmed in MS Excel – setting Hong Kong
- Erlotinib versus gefitinib



Diagnoses of obscure GI
Bleeding via Capsule Endoscopy

To analyze the cost-effectiveness of capsule endoscopy in diagnosing obscure gastrointestinal bleeding from a health care payer perspective in Germany



Objective

- ✦ To analyze the cost-effectiveness of capsule endoscopy compared to push enteroscopy in diagnosing obscure gastrointestinal bleeding (OGIB) from a health care payer perspective in Germany (France, the United Kingdom and Switzerland).

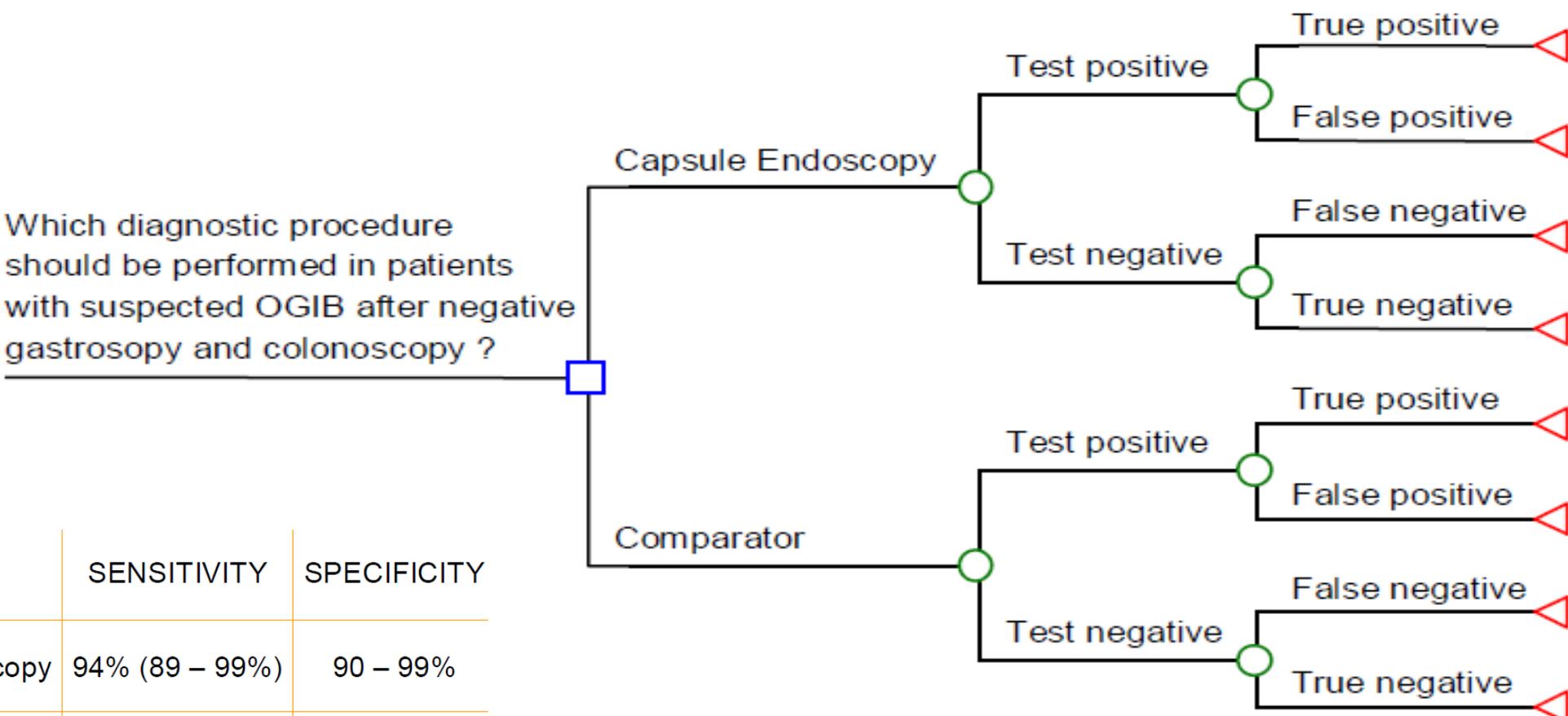
Data Basis

- ✦ 7 controlled clinical trials following the same study protocol; n = 184 patients with OGIB and previous negative gastroscopy and negative colonoscopy.
- ✦ Effectiveness parameters: sensitivity and specificity.
- ✦ Key difficulty was that the TRUE prevalence of OGIB was not known as the trials were not using the gold-standard comparator (intraoperative enteroscopy).

Modeling Methodology

- ✦ Decision tree model incorporating first and second-order Monte Carlo simulation programmed using the TreeAge software.

The model uses a general decision analytic approach in order to determine the diagnostic outcomes and the related costs of capsule endoscopy and its comparator



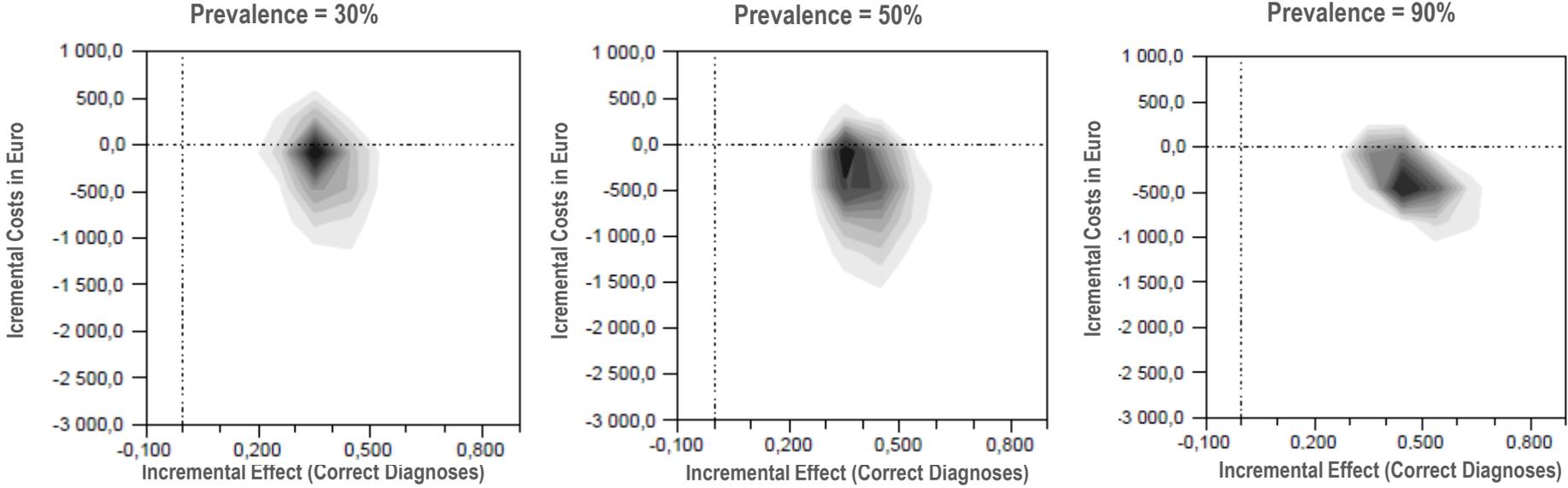
	SENSITIVITY	SPECIFICITY
Capsule Endoscopy	94% (89 – 99%)	90 – 99%
Push Enteroscopy	53% (27 – 60%)	50 – 70%

Capsule endoscopy is cost saving - the dominant strategy – in Germany, i.e. more effective and less costly compared to push enteroscopy if the prevalence of OGIB is 30% or higher



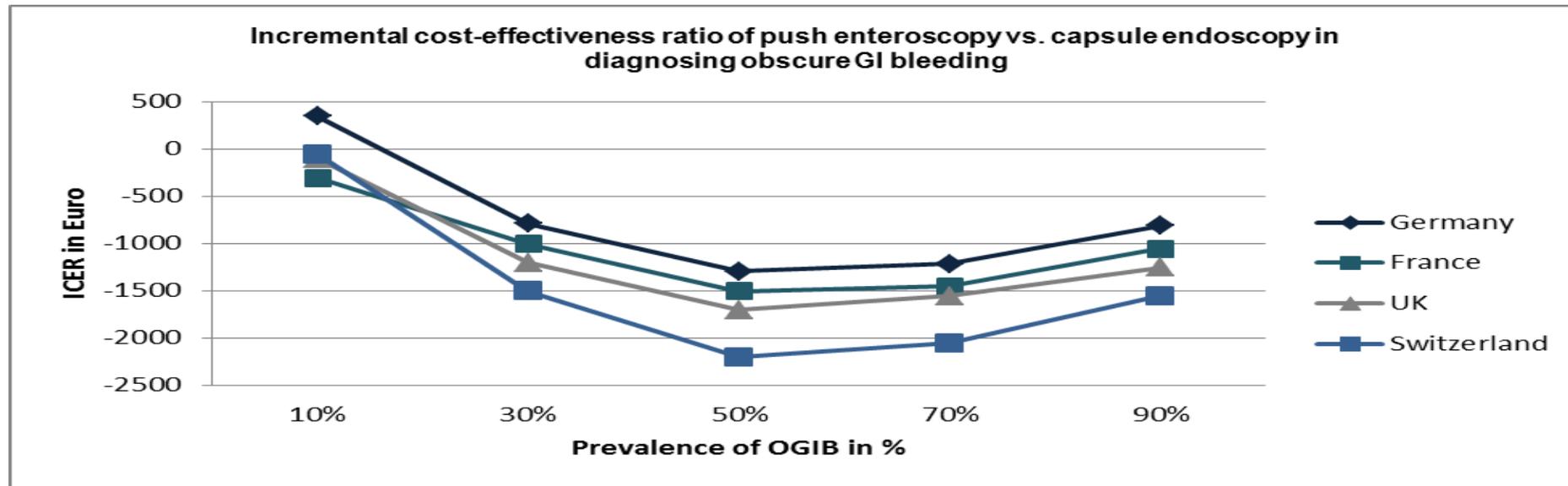
Prevalence	Push Enteroscopy		Capsule Endoscopy		Incremental		
	Costs	Effect	Costs	Effect	Costs	Effect	CE
10%	962,86	0,6035	1.081,85	0,9417	118,99	0,3382	351,83
30%	1.415,46	0,5730	1.125,11	0,9428	-290,35	0,3698	-785,15
50%	1.665,70	0,5424	1.148,09	0,9439	-517,61	0,4015	-1.289,19
70%	1.672,13	0,5118	1.146,67	0,9450	-525,46	0,4332	-1.212,97
90%	1.501,49	0,4813	1.127,54	0,9461	-373,95	0,4648	-804,54

Effect = proportion of correct diagnoses (true positive plus true negative diagnoses)



Look, Move & Stay AHEAD

Adaptations of the model for the healthcare settings of France, the UK and Switzerland showed even better results than those observed for Germany



References

- ❖ Mueller E, **Schwander B**, Bergemann R: Use of Capsule Endoscopy in Diagnosing Obscure Gastrointestinal Bleeding: Cost-Effectiveness Evaluation from a European Perspective; ISPOR 7th European Congress, Hamburg, Germany, October 2004 (PGI4)
- ❖ Mueller E, **Schwander B**, Bergemann R. Cost-effectiveness evaluation for a new diagnostic test considering also costs for false negative and false positive diagnoses at various prevalence rates; ISPOR 7th European Congress, Hamburg, Germany, October 2004 (PGI14)
- ❖ Mueller E; **Schwander B**; Zerwes U, Bergemann R: HTA Bericht: [Klinische und ökonomische Evaluation des diagnostischen Verfahrens "Kapselendoskopie" zur Untersuchung des Dünndarms](#); DIMDI DAHTA-Datenbank; Dokument-Nr. DAHTA107, Berichts-Nr. ANALYTICA002, September 2004

Key Takeaways for the client – capsule endoscopy



- Capsule endoscopy is more efficacious compared to push enteroscopy in diagnosing obscure gastrointestinal bleeding (OGIB) after negative gastro- and colonoscopy.
- Capsule endoscopy is cost-saving in all four countries analyzed (Germany, France, UK and Switzerland).
- **Key Message: Capsule endoscopy is the dominant strategy (more efficacious and less costly) compared to push enteroscopy and should hence become the standard of care for diagnosing OGIB (after negative gastro- and colonoscopy).**



Sequential Therapy in Renal Cell Carcinoma

To provide evidence for the superiority of the therapy sequence starting with first-line bevacizumab in renal cell carcinoma



Objective

- ✦ The novel targeted agents bevacizumab (BEV), sorafenib (SOR), sunitinib (SUN), everolimus (EVR) and pazopanib (PAZ) have each demonstrated activity in metastatic renal-cell carcinoma (mRCC) patients.
- ✦ Which therapy sequence provides the most valuable outcome in terms of progression-free survival (PFS) and overall survival (OS)?

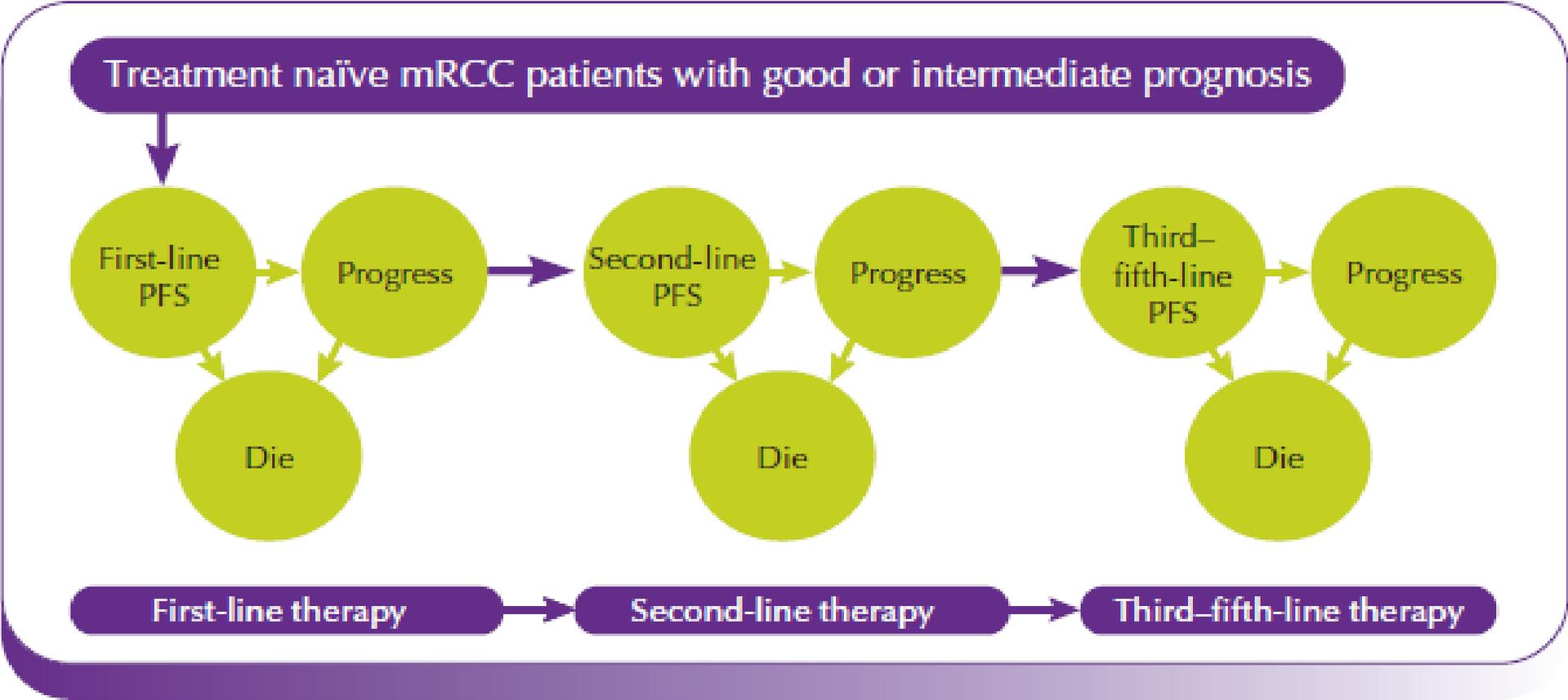
Data Basis

- ✦ The mRCC sequencing model has been based on the highest evidence available using pivotal phase-III trial outcomes from 1st and 2nd-line studies.
- ✦ From 3rd-line onwards the 2nd-line risks of progression and mortality have been applied as clinical trial evidence for therapy sequencing is still limited.

Modeling Methodology

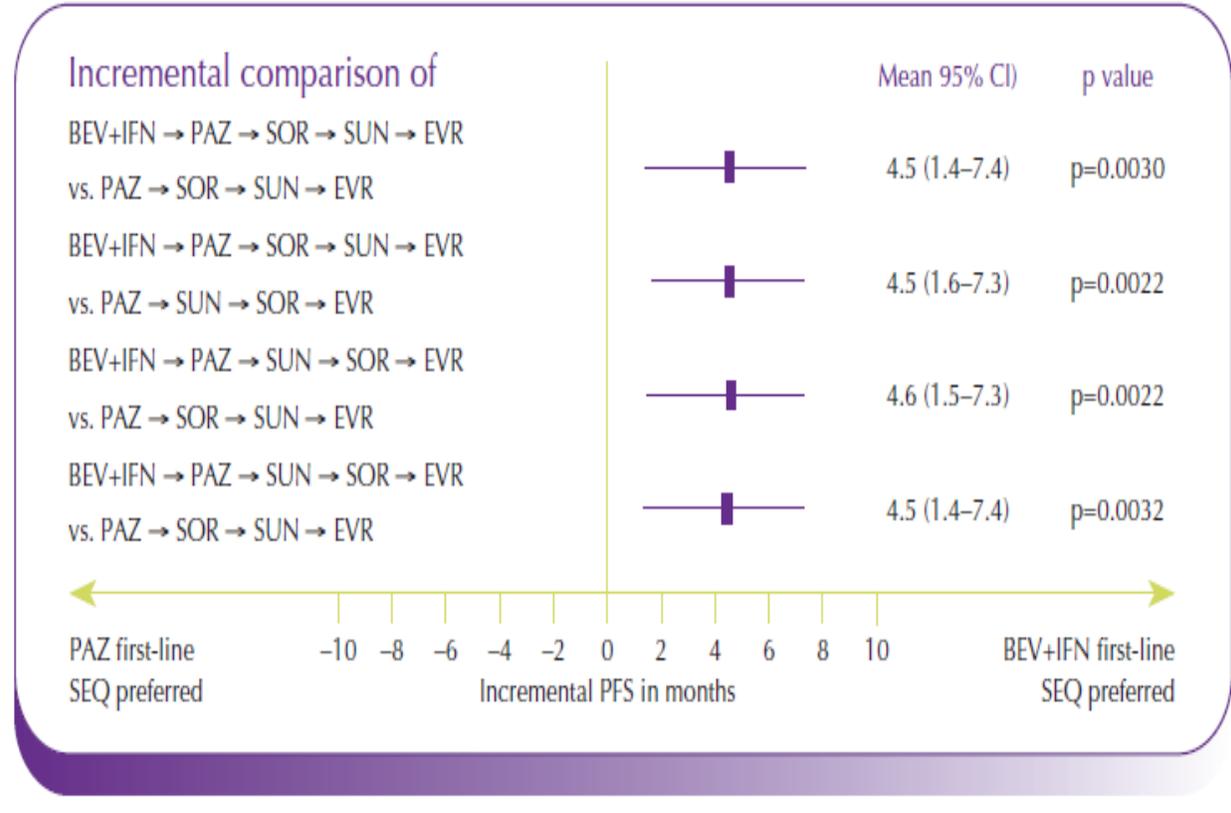
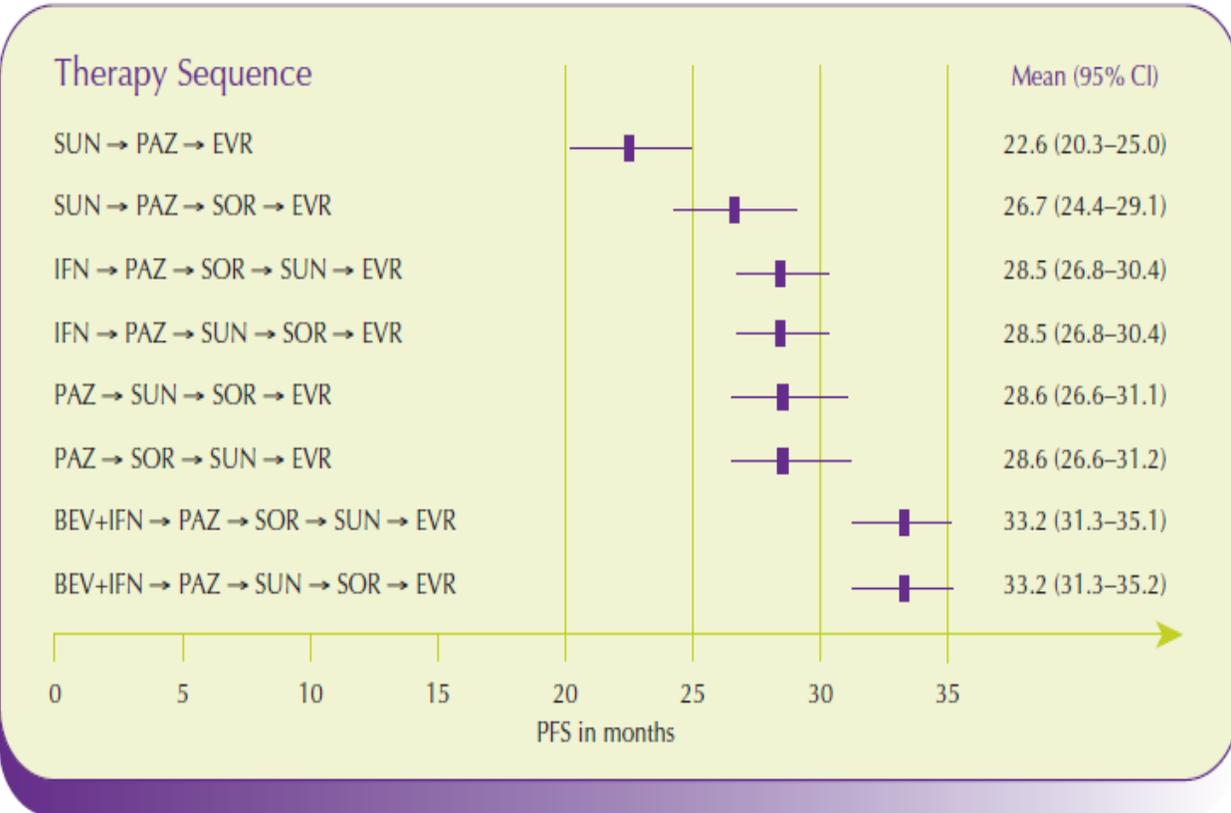
- ✦ Object-oriented probabilistic Monte Carlo simulation model based on a Markov process with first- and second-order calculations.
- ✦ The model was developed using the Excel-Add-In of the TreeAge software.

The aim of the Markov model is to estimate and compare the health benefits, expressed as total progression-free life months and total life months, of various recommended therapy sequences in mRCC



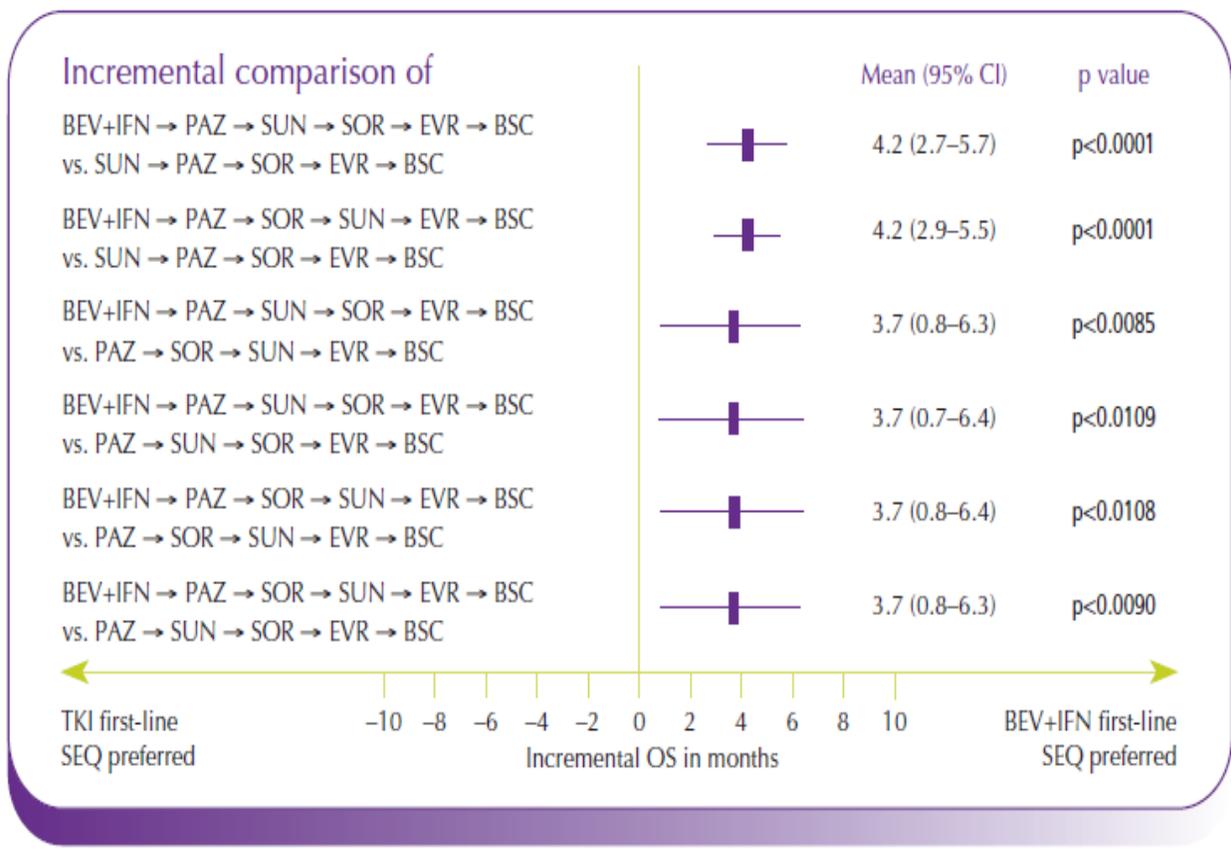
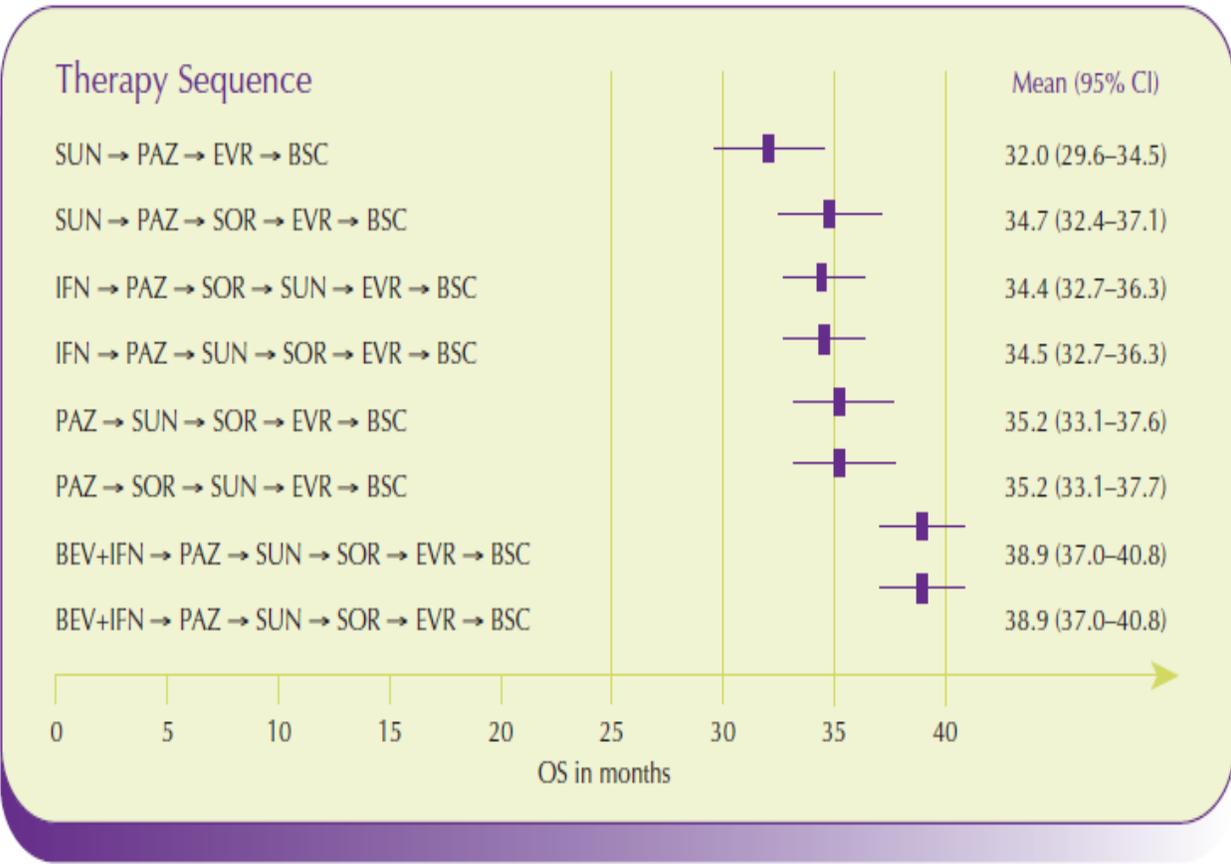
Source: Mickisch GH, Schwander B, Cassinello JG, Carles J, Walzer S, Nuijten M: Simulation and Comparison of Progression-Free Survival Outcomes of Sequential Therapy in Metastatic Renal-Cell Carcinoma; ISPOR 13th Annual European Congress Prague, Czech Republic, November 2010 (PCN 23)

Modeling results for the PFS in months of the first-line BEV+IFN sequence vs. others indicate that there is strong evidence for a statistically significant superiority of the 1st-line BEV+IFN sequence



Source: Mickisch GH, Schwander B, Cassinello JG, Carles J, Walzer S, Nuijten M: Simulation and Comparison of Progression-Free Survival Outcomes of Sequential Therapy in Metastatic Renal-Cell Carcinoma; ISPOR 13th Annual European Congress Prague, Czech Republic, November 2010 (PCN 23)

Modeling results for the OS in months of the first-line BEV+IFN sequence vs. others indicate that there is strong evidence for a statistically significant superiority of the 1st-line BEV+IFN sequence



Source: Mickisch GH, Schwander B, Cassinello JG, Carles J, Walzer S, Nuijten M: Simulation and Comparison of Progression-Free Survival Outcomes of Sequential Therapy in Metastatic Renal-Cell Carcinoma; ISPOR 13th Annual European Congress Prague, Czech Republic, November 2010 (PCN 23)

Modeling simulation indicates that patient PFS and OS outcomes could be improved significantly if therapy is started with first-line BEV+IFN, compared with other first-line agents



SIMULATION AND COMPARISON OF PROGRESSION-FREE-SURVIVAL OUTCOMES OF SEQUENTIAL TARGETED THERAPY IN METASTATIC RENAL-CELL CARCINOMA
G.H.J. Mickisch, B. Schwander, J.G. Cassinello, J. Carles, S. Walzer, M. Nuijten

Abstract
The aim of this study was to compare the progression-free survival (PFS) outcomes of sequential targeted therapy (TT) regimens in metastatic renal cell carcinoma (mRCC) using a simulation model. The model was based on clinical trial data and was used to simulate the PFS outcomes of sequential TT regimens. The results show that the PFS outcomes of sequential TT regimens are significantly improved compared with other first-line agents.

Objectives
The objectives of this study were to compare the PFS outcomes of sequential TT regimens in mRCC using a simulation model. The model was based on clinical trial data and was used to simulate the PFS outcomes of sequential TT regimens.

Methods
The simulation model was based on clinical trial data and was used to simulate the PFS outcomes of sequential TT regimens. The model was based on clinical trial data and was used to simulate the PFS outcomes of sequential TT regimens.

Results
The results show that the PFS outcomes of sequential TT regimens are significantly improved compared with other first-line agents.

Conclusions
The results show that the PFS outcomes of sequential TT regimens are significantly improved compared with other first-line agents.

Key Message: Using bevacizumab plus interferon (BEV+IFN) as first-line therapy in renal cell carcinoma improves patient outcomes in terms of PFS and OS if simulating the whole therapy sequence.

Reference

Mickisch GH, Schwander B, Cassinello JG, Carles J, Walzer S, Nuijten M: Simulation and Comparison of Progression-Free Survival Outcomes of Sequential Therapy in Metastatic Renal-Cell Carcinoma; ISPOR 13th Annual European Congress Prague, Czech Republic, November 2010 (PCN 23)



Antihypertensive Therapy – Primary & Secondary Prevention

To investigate the cost-utility of eprosartan versus enalapril (primary prevention) and versus nitrendipine (secondary prevention) in Germany



Objective

- ✦ To investigate the cost-utility of eprosartan versus enalapril (primary prevention) and versus nitrendipine (secondary prevention) on the basis of head-to-head evidence from randomized controlled trials.
- ✦ Healthcare settings Germany (Belgium, Norway , Spain, Sweden and the UK).

Data Basis

- ✦ Primary Prevention: Framingham-based risk calculation using systolic blood pressure reductions to estimate the relative risk reduction of cardiovascular and cerebrovascular events based on recent meta-analyses.
- ✦ Secondary prevention: an additional risk reduction is modeled for eprosartan according to the results of the MOSES study.

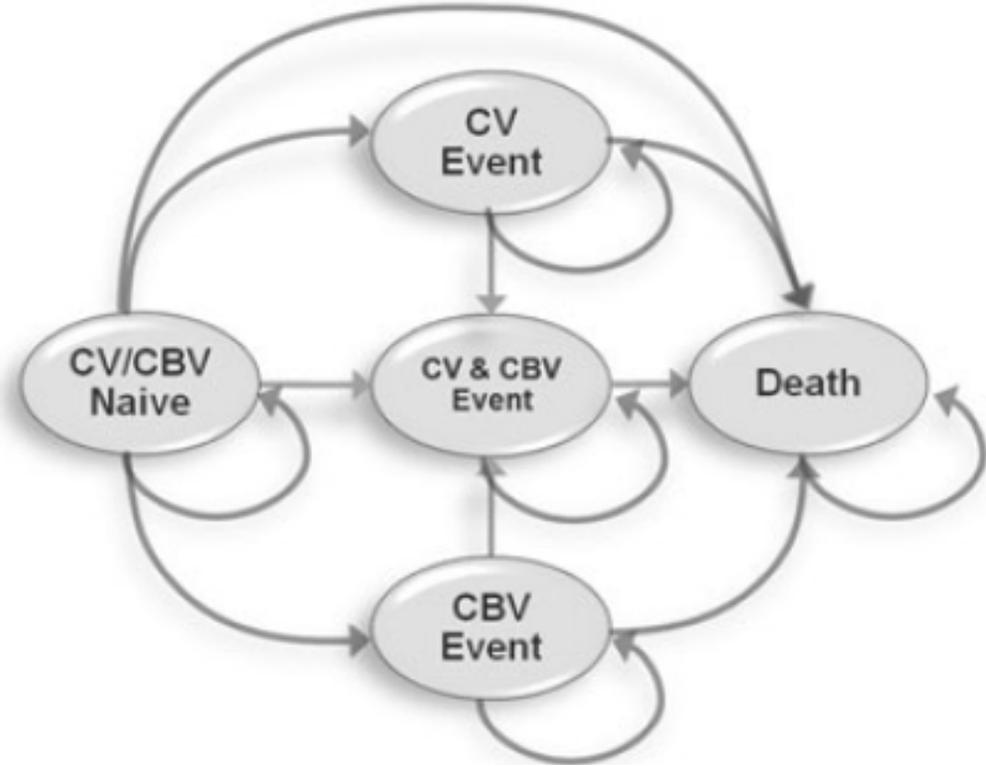
Modeling Methodology

- ✦ Object-oriented probabilistic Monte Carlo simulation model based on a Markov process with first- and second-order calculations.
- ✦ The model was developed using Delphi and C++.

The HEALTH model (Health Economic Assessment of Life with Teveten® for Hypertension) is an object-oriented probabilistic Monte Carlo simulation model



- ❖ The main Markov health states simulated by the model are “CV & CBV naive” (starting stage for the primary prevention population), “CV events,” “CBV events” (starting stage for the secondary prevention population), and “Death.”
- ❖ The “CV event” state is further classified in MI, AP, and other CV events and the “CBV event” state is further classified in stroke, TIA, and other CBV events.



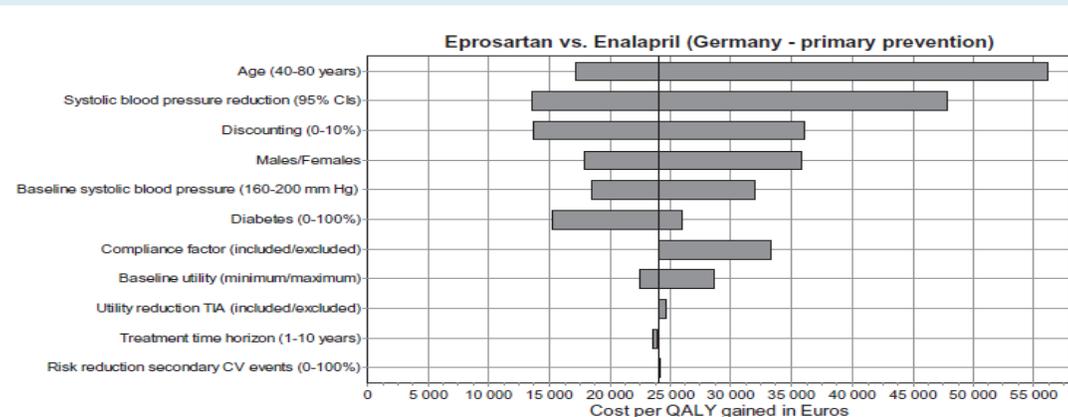
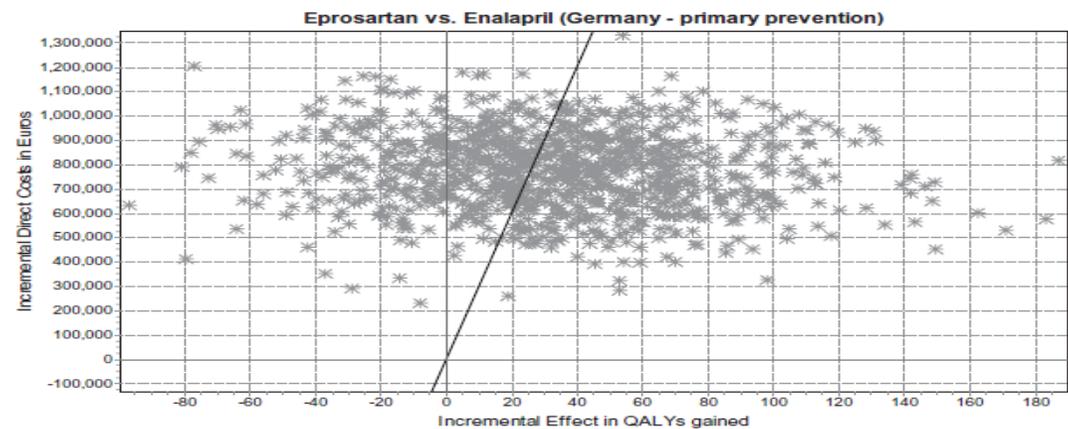
CV = Cardiovascular; CBV = cerebrovascular; MI = Myocardial Infarction; AP= Angina Pectoris. TIA = transient ischemic attack

Source: Schwander B, Gradl B, Zöllner Y, Lindgren P, Diener HC, Lüders S, Schrader J, Villar FA, Greiner W, Jönsson B: [Cost-utility analysis of eprosartan compared to enalapril in primary prevention and nitrendipine in secondary prevention in Europe - The Health Model](#); Value in Health 2009 Vol 12 (6): 857-870

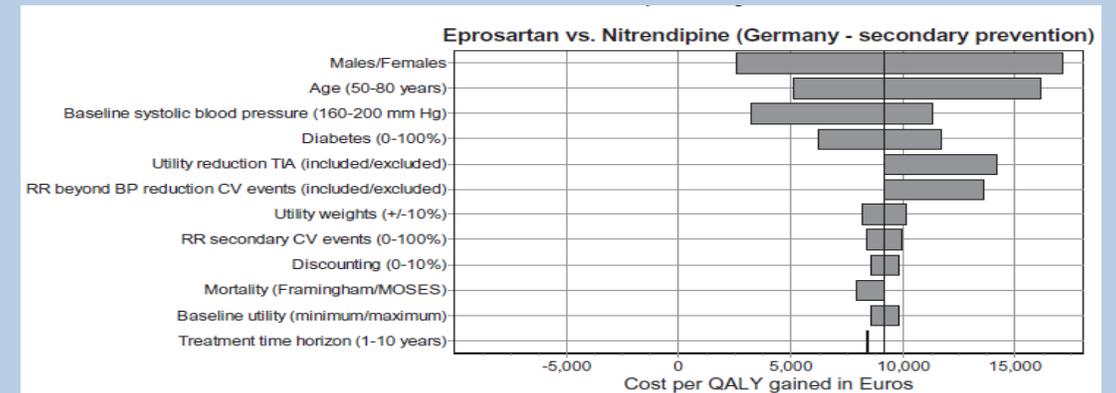
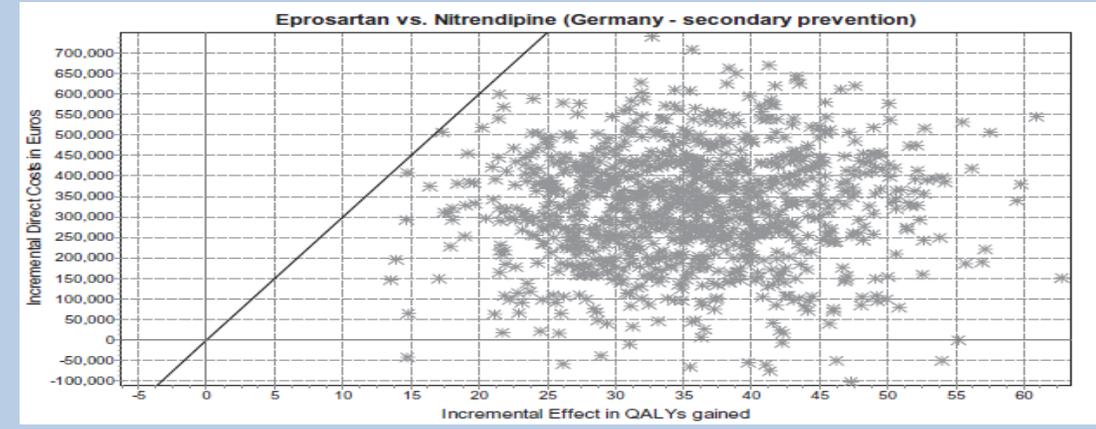
Considering a €30,000 willingness-to-pay threshold per QALY gained, eprosartan is cost-effective in primary prevention and cost-effective in secondary prevention in Germany



Primary Prevention



Secondary Prevention

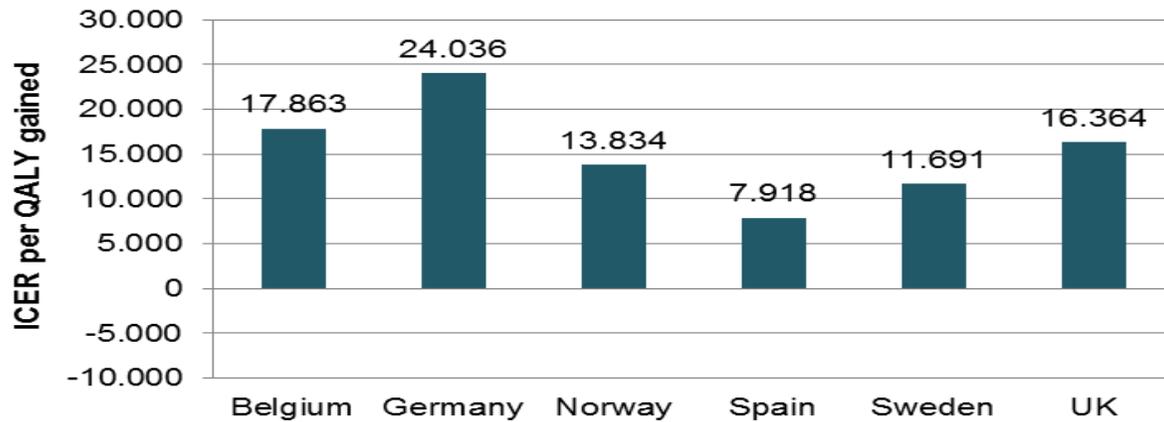


Source: Schwander B, Gradl B, Zöllner Y, Lindgren P, Diener HC, Lüders S, Schrader J, Villar FA, Greiner W, Jönsson B: [Cost-utility analysis of eprosartan compared to enalapril in primary prevention and nitrendipine in secondary prevention in Europe - The Health Model](#); Value in Health 2009 Vol 12 (6): 857-870

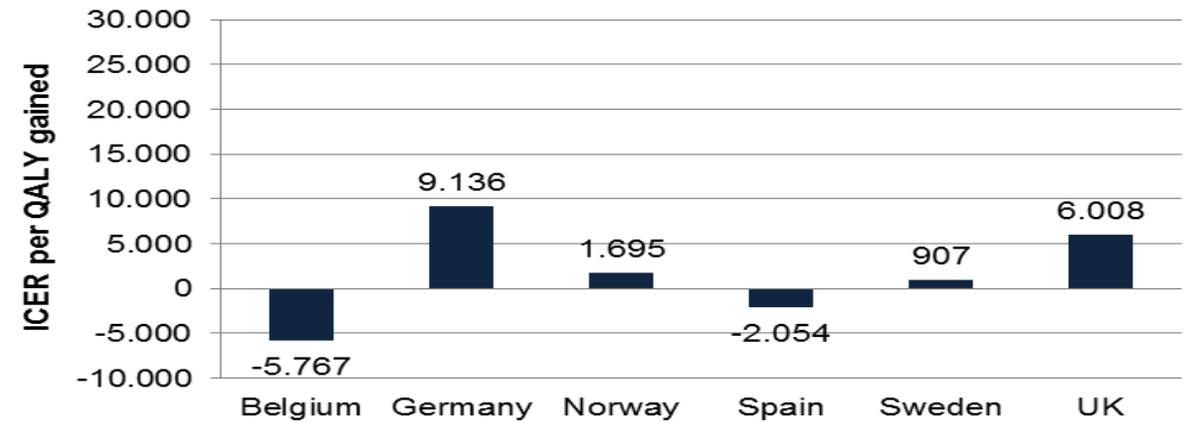
Adaptations of the model for the healthcare settings of Belgium, Norway, Spain, Sweden and the UK showed even better results than those observed for Germany



Primary Prevention: Cost per QALY gained comparing eprosartan vs. enalapril



Secondary Prevention: Cost per QALY gained comparing eprosartan vs. nitrendipine



References

- ✦ **Schwander B**, Gradl B, Zöllner Y, Lindgren P, Diener HC, Lüders S, Schrader J, Villar FA, Greiner W, Jönsson B: [Cost-utility analysis of eprosartan compared to enalapril in primary prevention and nitrendipine in secondary prevention in Europe - The Health Model](#); Value in Health 2009 Vol 12 (6): 857-870
- ✦ **Schwander B**, Lindgren P, Gradl B: The cost-effectiveness (cost-utility) of eprosartan in hypertensive patients with cerebrovascular disease in Belgium, Germany, Spain, UK, and Sweden; ISPOR 10th European Congress, Dublin, Ireland, October 2007 (CV8)
- ✦ **Schwander B**, Haller H. Eprosartan - Gesundheitsökonomische Betrachtung; Antihypertensive Schlaganfallprophylaxe und gesundheitsökonomische Aspekte; German Society for Internal Medicine; 113th Annual Meeting, Wiesbaden, Germany, April 2007
- ✦ Lindgren P, **Schwander B**, Zöllner Y, Jönsson B: Cost-utility analysis of Eprosartan compared to Enalapril and Ramipril in the treatment of moderate to severe hypertension in Sweden; ISPOR 9th European Congress, Copenhagen, Denmark, October 2006 (PCV53)

Key Takeaways for the client – Eprosartan in hypertension



- **Primary Prevention:** Focusing on older patients (≥ 50 years of age) with a higher systolic blood pressure (≥ 160 mm Hg) was identified as reasonable patient selection criteria to ensure a cost-effective application of eprosartan within a primary prevention setting.
- **Secondary Prevention:** The cost-effectiveness outcomes show considerable evidence for the cost-effectiveness of eprosartan compared to nitrendipine within a secondary prevention population, without any limitation related to the patient selection.
- **Key Message:** Eprosartan is cost-effective as compared to enalapril in primary prevention (patients ≥ 50 years old and a systolic blood pressure ≥ 160 mm Hg) and cost-effective as compared to nitrendipine in secondary prevention (all patients).



Therapy in EGFR MuT+ Non-Small Cell Lung Cancer

To compare the effectiveness and cost-effectiveness of erlotinib vs. gefitinib in first-line treatment EGFR MuT+ non-small cell lung cancer (NSCLC) for Hong Kong



Objective

- ✦ To compare the effectiveness and cost-effectiveness of erlotinib vs. gefitinib in first-line treatment of epidermal growth factor receptor (EGFR) activating-mutation positive (MuT+) non-small cell lung cancer (NSCLC) for Hong Kong

Data Basis

- ✦ In total four relevant Asian phase-III randomized controlled trials (RCTs) were determined: one for erlotinib (OPTIMAL) and three for gefitinib (IPASS; NEJGSG, WJTOG).
- ✦ The best fit of study characteristics and of prognostic patient characteristics were found between the OPTIMAL and IPASS trials.

Modeling Methodology

- ✦ An indirect treatment comparison (ITC) and a cost-effectiveness assessment (CEA) were performed.
- ✦ The ITC uses the Bucher et al. methodology and the CEA model is based on a Markov process (both were programmed in MS Excel).

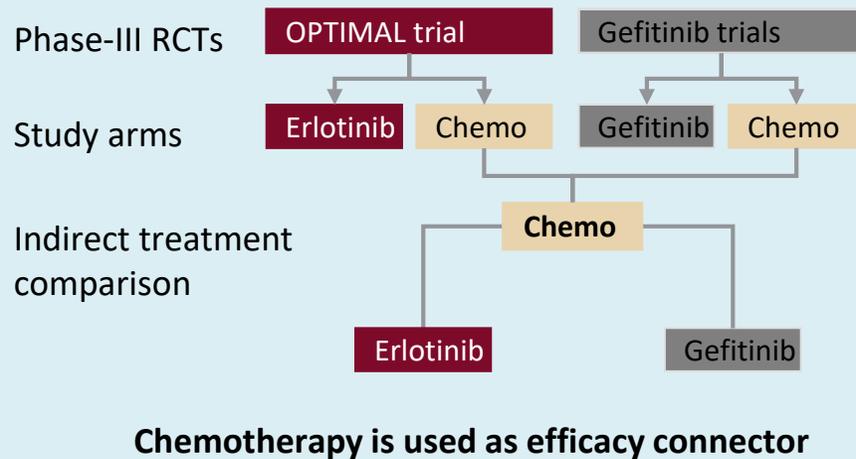
An indirect treatment comparison (ITC) and a cost-effectiveness assessment (CEA) were performed



ITC

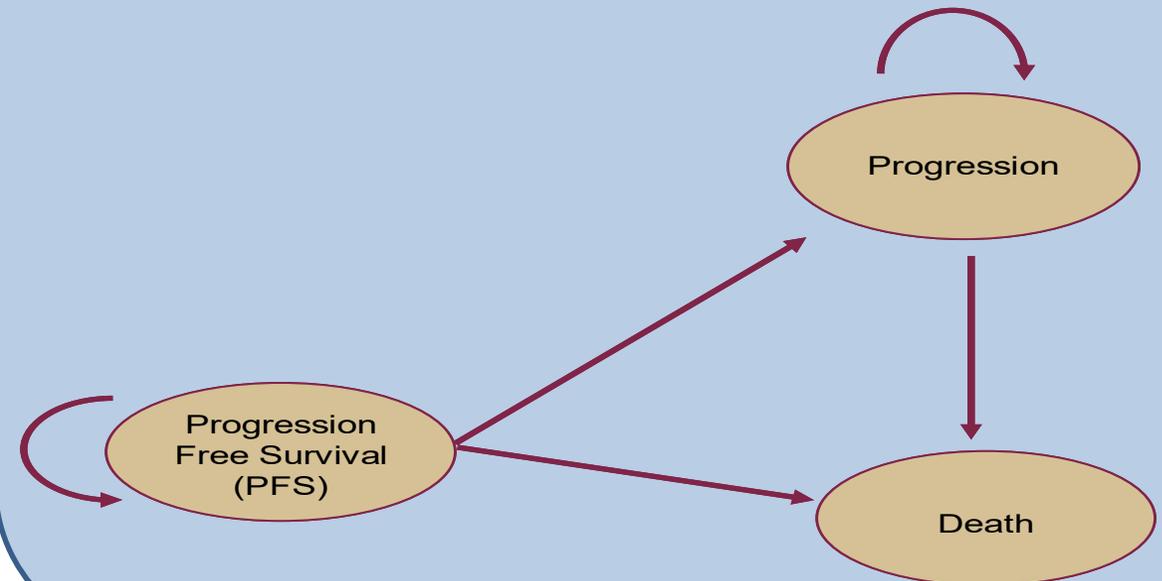
The ITC uses the Bucher method: the chemotherapy comparator arm of each trial has been used as a “bridge” to connect and compare the efficacy of the investigational treatment arms, namely erlotinib and gefitinib..

Erlotinib vs. gefitinib



CEA

The CEA model uses a Markov approach that simulates the transition between the health states: PFS, progression and death, in monthly cycles and over a life-time horizon.



Source: Lee VWY, Lee V, **Schwander B**: Comparative Effectiveness and Cost-Effectiveness Assessment of Erlotinib versus Gefitinib in First-Line Treatment of EGFR Activating Mutation Positive Non-Small Cell Lung Cancer for Hong Kong; poster presentation (PCN21) at the ISPOR 5th Asia Pacific Conference, Taipei, Taiwan, September 2012

Comparing the PFS HRs of erlotinib vs. gefitinib in first-line EGFR MuT+ NSCLC based on OPTIMAL and IPASS resulted in a statistically significant PFS difference in favor of erlotinib



ITC erlotinib vs. gefitinib

ITC HR (95%CI) p-value

Erlotinib vs. single-trial gefitinib evidence

OPTIMAL vs. IPASS

0.33 (0.20-0.56) p<0.0001

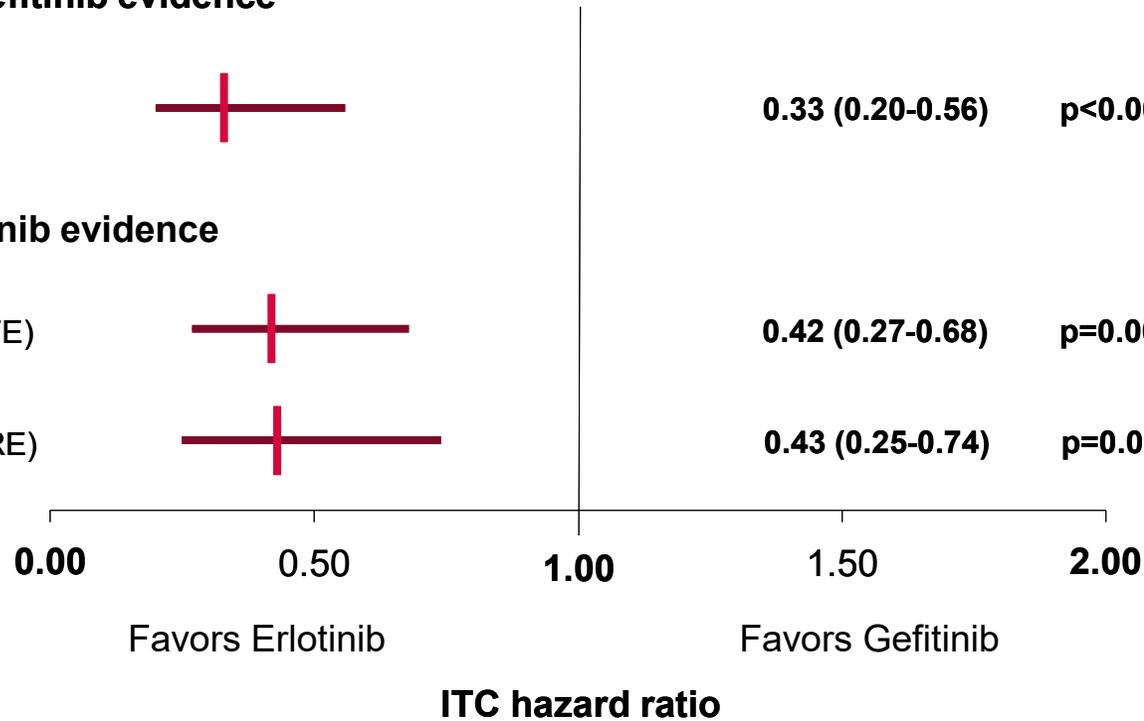
Erlotinib vs. pooled gefitinib evidence

OPTIMAL vs. pooled gefitinib (FE)

0.42 (0.27-0.68) p=0.0004

OPTIMAL vs. pooled gefitinib (RE)

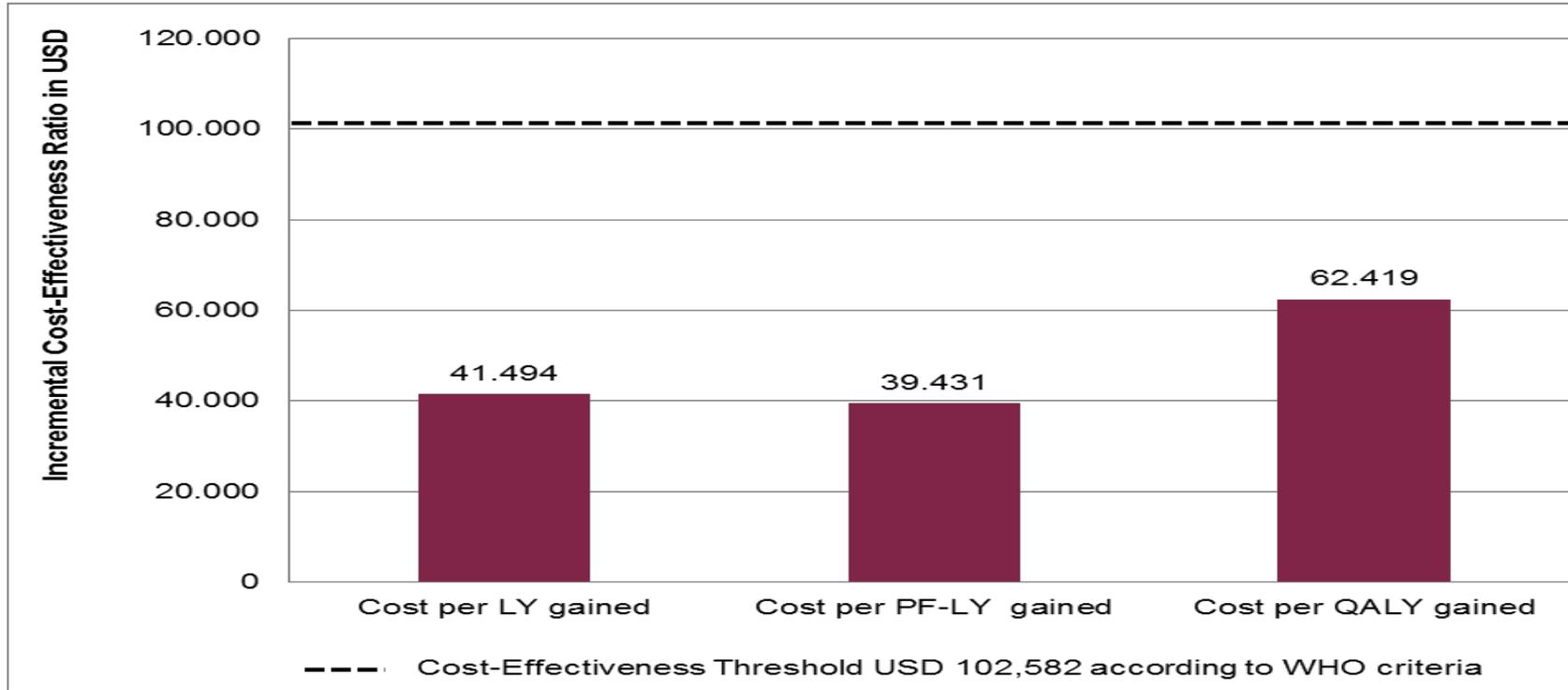
0.43 (0.25-0.74) p=0.0024



ITC HR=Indirect Treatment Comparison Hazard Ratio; RE=Random Effect Pooling; FE=Fixed Effect Pooling;

Source: Lee VWY, Lee V, Schwander B: Comparative Effectiveness and Cost-Effectiveness Assessment of Erlotinib versus Gefitinib in First-Line Treatment of EGFR Activating Mutation Positive Non-Small Cell Lung Cancer for Hong Kong; poster presentation (PCN21) at the ISPOR 5th Asia Pacific Conference, Taipei, Taiwan, September 2012

The CEA shows that the cost per LY gained, the cost per PF-LY gained and the cost per QALY gained by erlotinib are well within an acceptable range in relation to the survival benefit obtained



LY = Life Year; PF-LY = Progression-Free Life Year; QALY = Quality Adjusted Life Year

Reference

- Lee VWY, Lee V, **Schwander B**: Comparative Effectiveness and Cost-Effectiveness Assessment of Erlotinib versus Gefitinib in First-Line Treatment of EGFR Activating Mutation Positive Non-Small Cell Lung Cancer for Hong Kong; poster presentation (PCN21) at the ISPOR 5th Asia Pacific Conference, Taipei, Taiwan, September 2012

Key Takeaways for the client – erlotinib in NSCLC



- The comparative effectiveness assessment of OPTIMAL and IPASS shows that erlotinib is more efficacious when indirectly compared to gefitinib.
- The cost effectiveness assessment for Hong Kong shows that the cost per life year gained, the cost per progression-free life year gained and the cost per quality-adjusted life year gained by erlotinib are well within an acceptable range in relation to the survival benefit obtained.
- **Key Message: Erlotinib is more efficacious and is cost effective (value for money) compared to gefitinib in 1L EGFR Mut+ NSCLC and should hence be the preferred therapy option in this setting.**



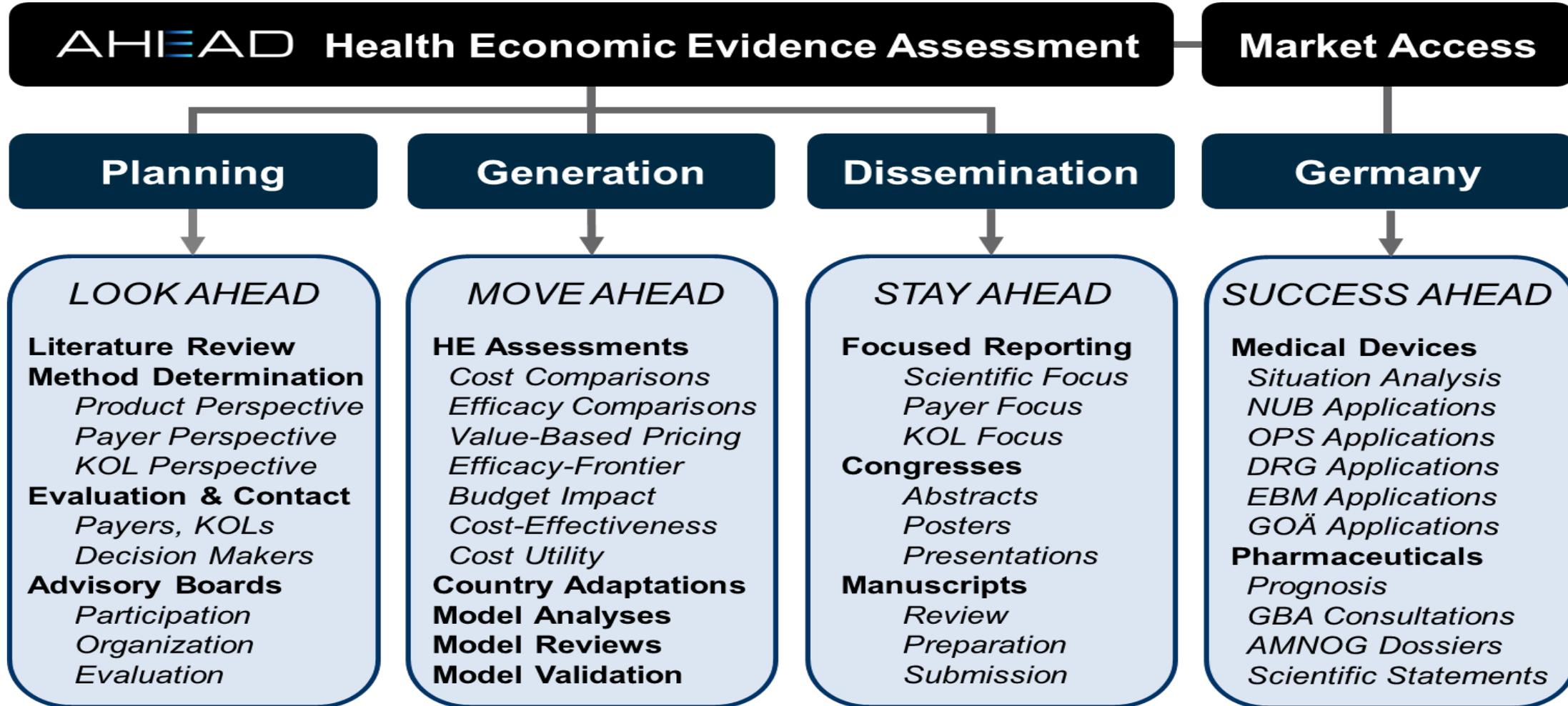
Market Access and Reimbursement in Germany

- ✦ **Market Access:** Evaluation and implementation of market access strategies and of reimbursement strategies for medical devices, pharmaceuticals and digital health solutions in Germany.

Global Health Economic Evidence Assessment

- ✦ **Planning:** Determination which health economic assessments are essential for your product from the market launch, the HTA/payer and the KOL/provider perspective.
- ✦ **Generation:** Development and application of health economic evaluations and/or models in order to generate the health economic evidence for your product.
- ✦ **Dissemination:** Communication of the health economic value messages (based on the health economic assessment results) to decision makers, payers, providers & KOLs.

The AHEAD philosophy is to provide **high-quality, product-specific and client-need-specific** consulting and research activities that will be **delivered on time**



We invite you to benefit from our more than 20 year experience in market access and health economic outcomes research in order to **bring your product AHEAD**



-  20+ years experience in health economics, HTA and market access
-  Founder & General Manager of AHEAD GmbH based in Germany
-  Nursing Diploma, Bachelor in Health Sciences, Master in Health Economics
-  Broad contract research, publishing, presentation and moderation experience



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