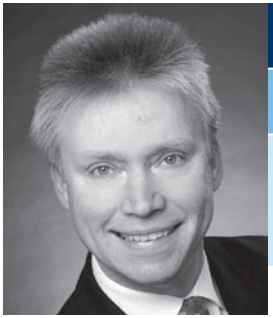


INTERVIEW

Martin Reck, MD, PhD

Dr Reck is Head of the Thoracic Oncology and Clinical Trial Departments at Hospital Grosshansdorf in Grosshansdorf, Germany.

Tracks 1-13

Track 1 Safety and mechanism of action of BIBF 1120: A novel triple angiokinase inhibitor

Track 2 Revisiting contraindications to the use of bevacizumab in patients with squamous cell disease

Track 3 A Phase II trial of ipilimumab and paclitaxel/carboplatin as first-line therapy for Stage IIIB/IV NSCLC

Track 4 Vaccine-based therapies under investigation in NSCLC

Track 5 **Case discussion:** A 44-year-old woman and never smoker who presents with EGFR-mutant, Stage IV, TTF-1-positive adenocarcinoma of the lung and diffuse bone metastasis exhibits a dramatic response to EGFR TKI therapy

Track 6 Management of the cutaneous side effects of EGFR TKIs in NSCLC

Track 7 Cisplatin/pemetrexed as salvage therapy for patients with metastatic NSCLC and acquired resistance to EGFR TKIs

Track 8 **Case discussion:** A 62-year-old woman with Stage IV adenocarcinoma of the lung with pleural, pericardial and brain metastases receives carboplatin/vinorelbine/bevacizumab on a clinical trial

Track 9 Safety of bevacizumab for patients with NSCLC and CNS metastases

Track 10 Assessment of EGFR mutation status in nonsmokers and smokers with NSCLC

Track 11 **Case discussion:** A 68-year-old man with squamous cell carcinoma of the lung and multiple comorbidities receives cisplatin-based chemotherapy followed by radiation therapy

Track 12 Use of erlotinib as second-line or maintenance therapy for squamous cell carcinoma of the lung

Track 13 Disparity in identification of targeted agents for adenocarcinoma and squamous NSCLC

Select Excerpts from the Interview

Track 1

DR LOVE: Would you comment on the novel anti-angiogenic agent BIBF 1120, which you've been involved in studying?

DR RECK: BIBF 1120 is an oral VEGF TKI somewhat comparable to bevacizumab in that its action is anti-angiogenic. Bevacizumab is a direct inhibitor of VEGF, and BIBF 1120 is a direct inhibitor of the VEGF receptor.

Beyond this, BIBF 1120 is also an inhibitor of the PDGF and FGF receptors, so it's inhibiting crucial structures that are responsible for angiogenesis.

We have performed a Phase II trial of single-agent BIBF 1120 for patients with relapsed advanced NSCLC (Reck 2011; [4.1]), and we will soon present Phase III data from a second-line trial in which we combined BIBF 1120 with docetaxel for patients with advanced NSCLC (4.2).

We can say based on 2 interim analyses that we received recommendation from the data monitoring committee to move forward with the trials. We haven't seen any severe safety risks associated with treatment with BIBF 1120. We were able to fully recruit the trial. We have closed the database and await the final data.

DR LOVE: Did you observe any anti-angiogenic-like side effects such as hypertension or nosebleeds?

DR RECK: We did see some hypertension. We also saw a minimal increase in proteinuria but no severe or significant increase in bleeding events, especially in hemoptysis. So, in contrast to bevacizumab, we included all histologies with BIBF 1120, not only nonsquamous NSCLC. We included patients with squamous cell disease, who are excluded from treatment with bevacizumab. We didn't observe any increase in severe bleeding events in this group of patients.

4.1

Phase II Study of the Triple Angiokinase Inhibitor BIBF 1120 for Patients with Relapsed Advanced Non-Small Cell Lung Cancer

Efficacy	BIBF 1120 (n = 73)*
Median progression-free survival (PFS)	6.9 weeks
Median overall survival	21.9 weeks
Tumor stabilization	46%
Safety (most commonly reported drug-related adverse events)	
Nausea	57.5%
Diarrhea	47.9%
Vomiting	42.5%
Anorexia	28.8%
Abdominal pain	13.7%

* Patients for whom first- or second-line platinum-based chemotherapy failed were randomly assigned to 250 mg or 150 mg of BIBF 1120 BID.

Conclusion:

Continuous treatment with BIBF 1120 was well tolerated, with no difference in efficacy between treatment arms. PFS and objective response with single-agent treatment in advanced disease warrants further exploration.

Reck M et al. *Ann Oncol* 2011;22(6):1374–81.

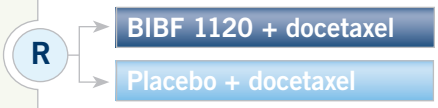
4.2

LUME Lung 1: A Randomized Phase III Trial of BIBF 1120 versus Placebo in Combination with Docetaxel for Patients with Advanced Non-Small Cell Lung Cancer (NSCLC)

Protocol ID: NCT00805194
Target Accrual: 1,300

Eligibility

- Locally advanced and/or metastatic NSCLC of Stage IIIB or IV or recurrent NSCLC
- Relapse or failure of 1 prior first-line chemotherapy
- ECOG PS 0 to 1



Primary endpoint: Progression-free survival

www.clinicaltrials.gov. Accessed December 2011.

Track 9

DR LOVE: What are your thoughts on the issue of bevacizumab administration for patients with central nervous system (CNS) metastasis?

DR RECK: When we first started administering bevacizumab, some cases of CNS complications occurred. However, we now have data from a meta-analysis that indicate no increase in CNS adverse events with the use of bevacizumab in patients with CNS metastases (Besse 2010).

The European registration authority has now removed the label restriction on CNS metastases with the use of bevacizumab, and I personally have treated 15 or 20 cases of CNS metastasis and never observed any CNS event caused by the use of bevacizumab. ■

SELECT PUBLICATIONS

Besse B et al. **Bevacizumab safety in patients with central nervous system metastases.** *Clin Cancer Res* 2010;16(1):269-78.

Hilberg F et al. **BIBF 1120: Triple angiokinase inhibitor with sustained receptor blockade and good antitumor efficacy.** *Cancer Res* 2008;68(12):4774-82.

Reck M et al. **A phase II double-blind study to investigate efficacy and safety of two doses of the triple angiokinase inhibitor BIBF 1120 in patients with relapsed advanced non-small-cell lung cancer.** *Ann Oncol* 2011;22(6):1374-81.

Reck M. **BIBF 1120 for the treatment of non-small cell lung cancer.** *Expert Opin Investig Drugs* 2010;19(6):789-94.

Santos ES et al. **Targeting angiogenesis from multiple pathways simultaneously: BIBF 1120, an investigational novel triple angiokinase inhibitor.** *Invest New Drugs* 2011;[Epub ahead of print].