The primary analysis of the study occurred when all patients had either progressed or had the primary endpoint achieved. Imprime PGG (a novel innate immune cell modulator) was found to significantly improve overall survival (OS) and progression-free survival (PFS) in previously untreated patients with stage IV non-squamous NSCLC when combined with standard of care chemotherapy and bevacizumab (a monoclonal antibody against VEGF). Bevacizumab, in combination with platinum-based chemotherapy, improved symptom control and OS. Combination therapy with Imprime PGG resulted in a 48% ORR compared to 23% ORR with chemotherapy plus cetuximab (another monoclonal antibody). Results from the independent, blinded review are reported for all efficacy endpoints.

**Background**

Lung cancer is the leading cause of cancer death worldwide. Despite advances in treatment, the median survival of patients with metastatic NSCLC is approximately 8.5 months. The role of immunotherapy in combination with chemotherapy and targeted therapy is emerging, with pembrolizumab and nivolumab demonstrated to improve survival in patients with PD-L1-positive tumors. Bevacizumab has been shown to accumulate in the tumor microenvironment and has the potential to increase tumor response and improve clinical outcomes for patients with NSCLC.

**Objectives**

The objective of this phase 2 trial was to evaluate the safety and efficacy of Imprime PGG in combination with standard of care chemotherapy and bevacizumab in previously untreated patients with stage IV non-squamous NSCLC.

**Methods**

This was a multicenter, open-label, randomized (2:1) phase 2 trial. Patients were randomized to receive Imprime PGG (2 mg/kg) administered intravenously on days 1 and 8 of a 21-day cycle for 4 cycles followed by maintenance every 3 weeks until progression, unacceptable toxicity, or patient withdrawal. Chemotherapy and bevacizumab were administered according to standard of care.

**Results**

A total of 120 patients were enrolled (60 Imprime PGG, 60 control). The main results included:

- **ORR:** 31.8% in the Imprime PGG group vs 10.0% in the control group, with 5.1% grade 3 or 4 events.
- **PFS:** Median PFS of 16.3 months in the Imprime PGG group vs 7.8 months in the control group.
- **OS:** Median OS of 27.6 months in the Imprime PGG group vs 21.2 months in the control group.
- **Duration of Response:** More patients in the Imprime PGG group than in the control group had ongoing responses at 12 months (27.2% vs 14.0%).

**Conclusions**

Combination therapy with Imprime PGG improved OS, PFS, and ORR compared to standard of care chemotherapy and bevacizumab. Increased levels of serum biomarkers upregulated by Imprime PGG were associated with prolonged survival. The trial was sponsored by Biothera (ClinicalTrials.gov NCT 00874107, EudraCT 2008-006780-37). Independent central radiology review was performed at VirtualScopics, Inc.

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[1] Background information.

**Corresponding Author**

Walburga Engel-Riedel, MD, PhD
Klinikum Rechts der Isar, Technical University Munich, Munich, Germany
Email: walburga.engelriedel@medizin.m-hoechst.de

**Authors**

1. Walburga Engel-Riedel, MD, PhD
2. Folker Schneller, MD
3. Martin Wolf, MD
4. Wolfgang Schuchter, MD
5. Bo Ma, MD
6. Paulette Mattsson, MD
7. Jamie Lowe, MD
8. Ada Braun, MD

Klinikum der Stadt Köln GmbH, Köln, Germany; Klinikum Rechts der Isar, Technical University Munich, Munich, Germany; Klinikum Kassel GmbH, Kassel, Germany; Krankenhaus Marthe-Maria Halé Dülau, Halle (Saale), Germany; brothor, Eagan, MN, United States of America