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Press Statement

Nippon Boehringer Ingelheim Co., Ltd.

Astellas Pharma Inc.

Safety of telmisartan affirmed with an analysis of 50,000 patients
Disagreement with the publication of Sipahi et al in *Lancet Oncology* June 2010

Ingelheim, 14 June 2010 - Telmisartan, an angiotensin receptor blocker, is one of the best researched drugs worldwide. It has been studied in clinical trials in more than 50,000 patients. Its positive safety profile has been confirmed also in a market exposure of 34.5 million patient years. Convincing safety data for patients with a high cardiovascular risk were collected in the three long-term outcome trials ONTARGET, PRoFESS and TRANSCEND which followed some of the patients for up to five years. Following rigorous assessment of the data from these studies it was concluded that there was no association with an increased risk of cancer in the telmisartan arms.

Sipahi et al published a meta-analysis in the June issue of Lancet Oncology, claiming that angiotensin receptor blockers (ARBs) used to lower hypertension are associated with a modestly increased risk of new cancer diagnosis. The finding is mainly based on the combination arm of telmisartan and ramipril, an angiotensin converting enzyme (ACE)-inhibitor, and not on the trial arms of each compound separately. Ramipril is not available in Japan.

Patient health and safety is the primary concern of Boehringer Ingelheim.
The company continually monitors safety data for all medical products.
Boehringer Ingelheim's comprehensive internal safety data analysis of primary data contradicts the conclusions about an increased risk of potential malignancies mentioned by Sipahi et al.

All studies[i] with telmisartan included patients with cardiovascular risk factors due to age and comorbidities. Specifically, in ONTARGET, with more than 25.000 patients, no statistically significant difference with respect malignancies was observed in patients treated with telmisartan vs ramipril. The one treatment arm in ONTARGET with combination of telmisartan and ramipril was associated with a modestly increased risk of malignancies.

In TRANSCEND, a 6,000 patient trial, the difference did not reach significance either. In the PRoFESS trial, another large-scale trial with more than 20,000 patients, the telmisartan arm showed fewer cases of malignancies than the placebo arm. Considering the analysis of all three trials an effect of telmisartan on malignancies was not observed.

"Our research efforts have centred on the need to protect patients, especially older patients from cardiovascular risks such as myocardial infarction or stroke. Telmisartan fulfills this need and has become a valuable treatment option in the management of hypertension and cardiovascular risk. Doctors and patients appreciate its excellent safety profile. Doctors and patients appreciate its excellent safety profile. In pre-clinical trials, clinical trials and day-to-day patient exposure with telmisartan, we have not seen any significant finding related to malignancies. Patients should consult with their physicians before making any decision regarding their antihypertensive therapy," said Prof. Dr Klaus Dugi, Corporate Senior Vice President Medicine at Boehringer Ingelheim.

Peer-reviewed meta-analyses of aggregate published data like Sipahi et al have their appropriate place in scientific research. However, these analyses have well-recognised limitations, such as combining study summaries rather than analyzing individual patient data.

Telmisartan is one of the most studied anti-hypertensives in clinical trials, which have all been made publically available. It is widely used as medication to lower blood pressure and protect patients against severe cardiovascular events such as myocardial infarction and stroke.

Notes to editors

Specifically, in ONTARGET, no statistically significant difference with respect to malignancies was observed in patients treated with telmisartan vs ramipril (HR 1.05, 95%CI 0.94, 1.16). In TRANSCEND, the difference did not reach significance either (HR 1.17, 95%CI 0.97, 1.41). In the PRoFESS trial the placebo arm showed more cases of malignancies than the telmisartan arm (HR 0.92, 95%CI 0.79, 1.06). *

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