

**Phase 2 Study of Lenvatinib in Patients With Advanced Hepatocellular Carcinoma**

Kenji Ikeda, MD,<sup>1</sup> Masatoshi Kudo, MD,<sup>2</sup> Seiji Kawazoe, PhD,<sup>3</sup> Yukio Osaki, MD,<sup>4</sup> Masafumi Ikeda, MD,<sup>5</sup> Takuji Okusaka, MD,<sup>6</sup> Toshiyuki Tamai, MSc,<sup>7</sup> Takuya Suzuki, MSc,<sup>7</sup> Takashi Hisai, MSc,<sup>7</sup> Seiichi Hayato, MSc,<sup>7</sup> Kiwamu Okita, MD,<sup>8</sup> Hiromitsu Kumada, MD<sup>1</sup>

<sup>1</sup>*Department of Hepatology, Toranomon Hospital, Tokyo, Japan;* <sup>2</sup>*Department of Gastroenterology and Hepatology, Kinki University School of Medicine, Osaka, Japan;* <sup>3</sup>*Department of Hepatobiliary and Pancreatology, Saga-Ken Medical Centre KOSEIKAN, Saga, Japan;* <sup>4</sup>*Department of Gastroenterology and Hepatology, Osaka Red Cross Hospital, Osaka, Japan;* <sup>5</sup>*Department of Hepatobiliary and Pancreatic Oncology, National Cancer Center Hospital East, Kashiwa, Japan;* <sup>6</sup>*Department of Hepatobiliary and Pancreatic Oncology, National Cancer Center Hospital, Tokyo, Japan;* <sup>7</sup>*Eisai Co., Ltd., Tokyo, Japan;* <sup>8</sup>*Shunan Memorial Hospital, Yamaguchi, Japan.*

**Corresponding author:**

Kenji Ikeda, MD

Department of Hepatology, Toranomon Hospital

Toranomon 2-2-2, Minato-ku, Tokyo 105-8470, Japan

Email: [ikedakenji@tora.email.ne.jp](mailto:ikedakenji@tora.email.ne.jp)

Telephone: +81-3-3588-1111

Fax: +81-3-3582-7068

**Online Resource Table S1: Dose Reduction Guidelines**

Drug-related AE Grades		Dose Delay	Dose Reduction to Restart
<b>HEMATOLOGIC TOXICITIES</b>			
Grade 4		Delay until ≤	Decrease 1 dose level <sup>a</sup>
Grade 3 thrombocytopenia that requires blood transfusion		Grade 2	
<b>NONHEMATOLOGIC TOXICITIES</b>			
AST/ALT > 10.0 x ULN		Delay until ≤ Grade 1 or baseline Grade <sup>b</sup>	Decrease 1 dose level <sup>a</sup>
Proteinuria	4+ in dipstick		
	If monitored 3+ proteinuria but not judged grade 3 in dipstick		
Hypertension: Grade 4 that is uncontrollable despite more intensive therapy than previously			
Diarrhea/vomiting/nausea: Grade 3 or higher that is uncontrollable despite maximal supportive therapies			
Any grade 3–4 nonhematologic toxicity other than above except for abnormal clinical laboratory values that require			

no treatment		
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<sup>a</sup>Reduction of lenvatinib dose: 12 mg → 8 mg → 4 mg → discontinue treatment.

<sup>b</sup>Baseline grade is defined as the data from the baseline period.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; ULN, upper limit of normal.

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