

## **ELECTRONIC SUPPLEMENTARY MATERIAL**

**Title:** Bintrafusp alfa, a bifunctional fusion protein targeting TGF- $\beta$  and PD-L1, in patients with esophageal adenocarcinoma: results from a phase 1 cohort

### **Authors:**

Benjamin Tan<sup>1</sup>, Adnan Khattak<sup>2</sup>, Enriqueta Felip<sup>3</sup>, Karen Kelly<sup>4</sup>, Patricia Rich<sup>5</sup>, Ding Wang<sup>6</sup>, Christoph Helwig<sup>7</sup>, Isabelle Dussault<sup>8</sup>, Laureen S. Ojalvo<sup>8</sup>, Nicolas Isambert<sup>9</sup>

<sup>1</sup>Washington University School of Medicine, St Louis, MO, USA; <sup>2</sup>Fiona Stanley Hospital, Perth, Australia; <sup>3</sup>Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), IOB-Quiron, UVic-UCC, Barcelona, Spain; <sup>4</sup>University of California Davis Comprehensive Cancer Center, Sacramento, CA, USA; <sup>5</sup>Cancer Treatment Centers of America, Atlanta, GA, USA; <sup>6</sup>Henry Ford Cancer Institute, Detroit, MI, USA; <sup>7</sup>Merck KGaA, Darmstadt, Germany; <sup>8</sup>EMD Serono Research & Development Institute, Inc., Billerica, MA, USA; an affiliate of Merck KGaA, Darmstadt, Germany, and <sup>9</sup>Poitiers University Hospital, Poitiers, France

### **Corresponding author:**

Nicolas Isambert

nicolas.isambert@chu-poitiers.fr

**Supplemental Table S1. Concordance between independent review committee–  
and investigator-assessed confirmed best overall responses**

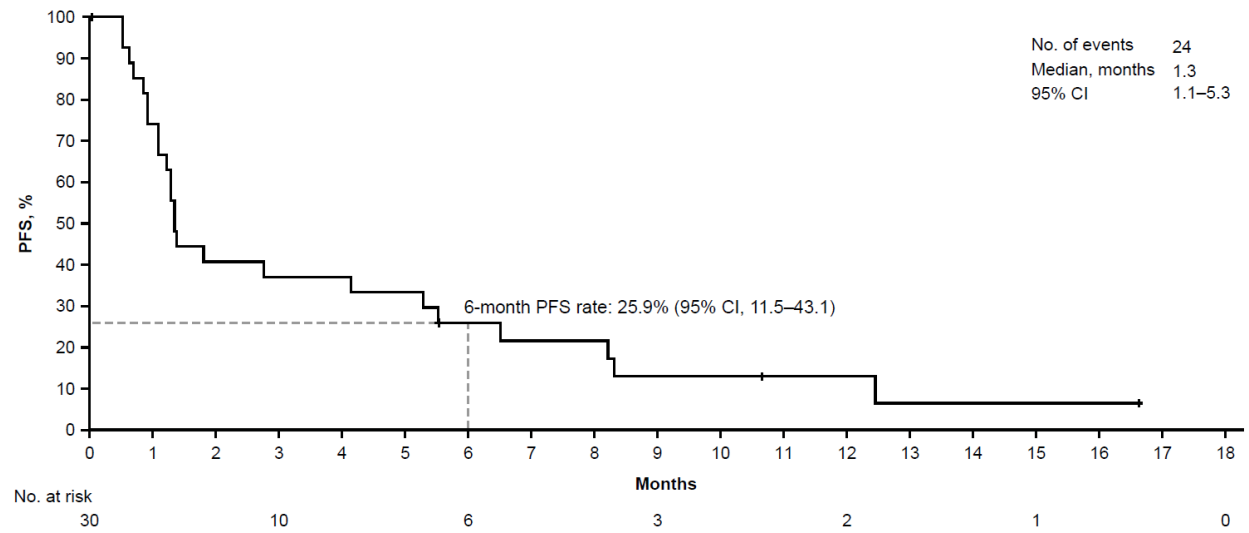
		Independent review committee, <i>n</i>						
		Complete response	Partial response	Stable disease	Progressive disease	Not evaluable		
Investigator, <i>n</i>	Complete response	0	0	0	0	0	0	Total, <i>n</i>
	Partial response	0	3	0	1	0	4	
	Stable disease	0	3	4	0	0	7	
	Progressive disease	0	0	0	12	0	12	
	Not Evaluable	0	0	0	2	5	7	
		0	6	4	15	5		
		Total, <i>n</i>						

**Supplemental Table S2. AEs of special interest**

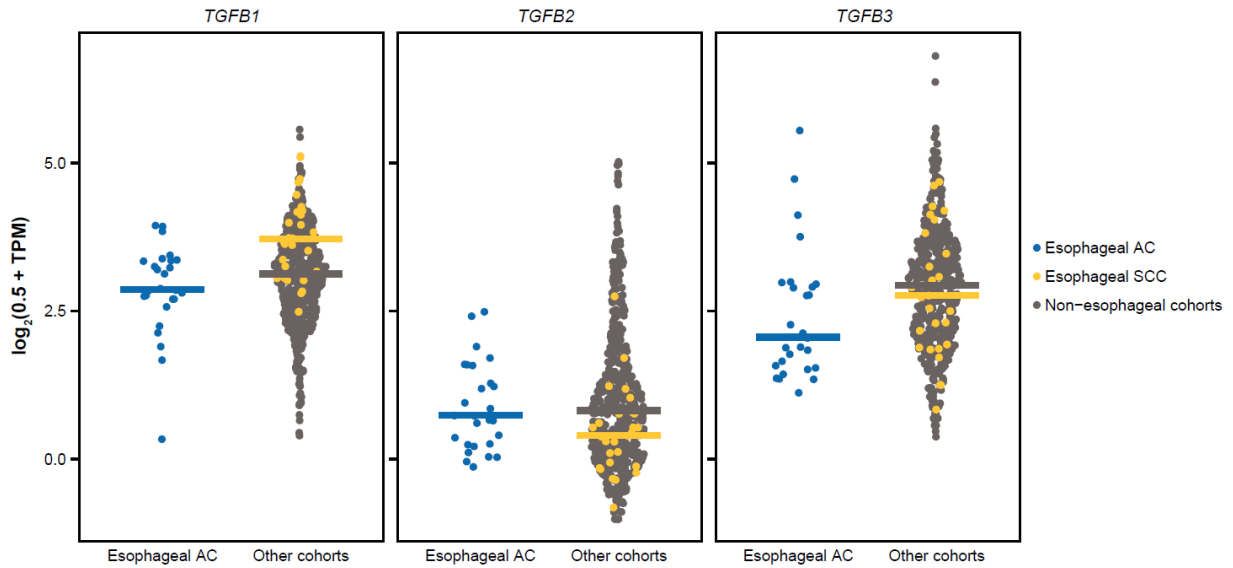
Preferred term, <i>n</i> (%)	<b>N=30</b>	
	<b>Any grade</b>	<b>Grade 3<sup>a</sup></b>
Any irAE	7 (23.3) <sup>b</sup>	2 (6.7)
Immune-related rash	5 (16.7)	1 (3.3)
Rash	2 (6.7)	0
Rash macular	2 (6.7)	0
Rash generalized	1 (3.3)	1 (3.3)
Pruritus	1 (3.3)	0
Immune-related pituitary dysfunction	1 (3.3)	1 (3.3)
Hypophysitis	1 (3.3)	1 (3.3)
Immune-related pneumonitis	1 (3.3)	0
Immune-related thyroid disorders	1 (3.3)	0
Hyperthyroidism	1 (3.3)	0
Hypothyroidism	1 (3.3)	0
Skin lesions <sup>c</sup>	2 (6.7) <sup>d</sup>	1 (3.3)
KA	2 (6.7)	0
Bowen's disease <sup>e</sup>	1 (3.3)	1 (3.3)
SCC of skin	1 (3.3)	1 (3.3)
Actinic keratosis	1 (3.3)	0
Hyperkeratosis	1 (3.3)	0

<sup>a</sup>No patients experienced a grade >3 event. <sup>b</sup>Three patients experienced multiple different irAEs. <sup>c</sup>Includes actinic keratosis, basal cell carcinoma, Bowen's disease, hyperkeratosis, KA, lip SCC, and SCC of skin NCI-CTCAE v4.03 preferred terms. <sup>d</sup>One patient experienced multiple different skin lesions. <sup>e</sup>Also known as SCC in situ. *AE* adverse event, *irAE* immune-related adverse event, *KA* keratoacanthoma, *SCC* squamous cell carcinoma, *TRAE* treatment-related adverse event.

**Supplemental Figure S1. Investigator-assessed Kaplan–Meier curve for progression-free survival (PFS)**



**Supplemental Figure S2. Expression of *TGFB1*, *TGFB2*, and *TGFB3* across phase 1 studies of bintrafusp alfa**



AC adenocarcinoma, SCC squamous cell carcinoma.