

# Chronic phase chronic myeloid leukemia patients with low OCT-1 activity randomized to high-dose imatinib achieve better responses and have lower failure rates than those randomized to standard-dose imatinib

Deborah L. White,<sup>1,2,3</sup> Jerald Radich,<sup>4</sup> Simona Soverini,<sup>5</sup> Verity A Saunders,<sup>1,2</sup> Amity K. Frede,<sup>1,2</sup> Phuong Dang,<sup>1,2</sup> Daniela Cilloni,<sup>6</sup> Peter Lin,<sup>4</sup> Lidia Mongay,<sup>7</sup> Richard Woodman,<sup>7</sup> Paul Manley,<sup>8</sup> Cassandra Slader,<sup>9</sup> Dong Wook Kim,<sup>10</sup> Fabrizio Pane,<sup>11</sup> Giovanni Martinelli,<sup>5</sup> Giuseppe Saglio,<sup>12</sup> and Timothy P. Hughes<sup>1,2,3</sup>

<sup>1</sup>Department of Haematology, SA Pathology (RAH Campus), Adelaide, Australia; <sup>2</sup>Centre for Cancer Biology, Adelaide, Australia; <sup>3</sup>Department of Medicine, Faculty of Health Science, University of Adelaide, Australia; <sup>4</sup>Fred Hutchinson Cancer Research Center, Seattle, WA, USA; <sup>5</sup>Department of Haematology/Oncology “L. e A. Seragnoli”, University of Bologna, Italy; <sup>6</sup>Department of Biology, University of Bologna, Bologna, Italy; <sup>7</sup>Novartis Oncology, Florham Park, NJ, USA; <sup>8</sup>Novartis Pharmaceuticals, Basel, Switzerland; <sup>9</sup>Novartis Oncology, Sydney, Australia; <sup>10</sup>The Catholic University of Korea, Seoul St Mary’s Hospital, Seoul, South Korea; <sup>11</sup>Division of Haematology, University of Naples “Federico II”, Naples, Italy, and <sup>12</sup>Department of Clinical and Biological Sciences, University of Turin, Orbassano, Italy

Citation: White DL, Radich J, Soverini S, Saunders VA, Frede AK, Dang P, Cilloni D, Lin P, Mongay L, Woodman R, Manley P, Slader C, Kim DW, Pane F, Martinelli G, Saglio G, and Hughes TP. Chronic phase chronic myeloid leukemia patients with low OCT-1 activity randomized to high-dose imatinib achieve better responses and lower failure rates than those randomized to standard-dose imatinib. *Haematologica* 2012;97(6):907-914. doi:10.3324/haematol.2011.056457

**Online Supplementary Table S1.** Baseline characteristics of the 100 patients analyzed in this study compared to those of the complete cohort of 476 patients in the TOPS study.

	Patients by randomized dose {Entire TOPS Cohort}					
	400mg (n=28)		800mg (n=72)		All (n=100)	
	N.	%	N.	%	N.	%
Age (years)	28	28 {32}	72	72 {67}	100	
Median	45 {45}		46 {48}		45.5 {47}	
Range	26-72 {18-75}		18-74 {18-75}		18-74 {18-75}	
Male sex	14	50 {53.5}	42	58 {57.4}	56	56 {56.1}

**Online Supplementary Table S2.** Dose demographics at 12 months for the 100 patients analyzed in this study compared to those observed in the entire TOPS cohort.

	400 mg arm {entire TOPS Cohort}	800 mg arm {entire TOPS Cohort}
Average dose intensity	384mg {388 mg}	679mg {662 mg}
Average dose intensity (range)	204-545mg {177-663 mg}	334-800mg {223-800 mg}
Average relative dose intensity	96% {97%}	84% {83%}
Breakdown of dose intensity*		≥750 mg 39/72 54% {>50%}
		≥793 mg 17/72 24% {25%}
		≥546 mg 55/72 76% {75%}

\* not reported for the 400mg arm of the entire TOPS cohort<sup>14</sup> thus, no comparison possible.

**Online Supplementary Table S3.** Response rates over time in the 100 patients analyzed in this study.

Variable	Patients by imatinib dose (randomized)						P value
	400 mg/day		800 mg/day				
	N. with response	N. evaluated	% of evaluated with response	N. with response	N. evaluated	% of evaluated with response	
<b>Major molecular reponse at different timepoints</b>							
At 6 months	4	28	14	31	72	43	0.008
At 9 months	10	28	36	42	72	58	0.024
At 12 months	15	28	54	45	72	62.5	0.143