

**eTable 5. Predictive performance of different definitions of progression independent of relapse activity against the risk of reaching EDSS score = 6.0 in 13432 patients with age  $\geq 37$  years and baseline EDSS  $\leq 5.5$**

Definition	Sensitivity	Specificity	NPV	PPV	Accuracy
B <sub>fix</sub> -24w-90d	72.3 (70.7-74.0)	24.0 (22.8-25.2)	59.9 (57.8-62.1)	35.6 (34.3-36.8)	41.8
B <sub>fix</sub> -24w-180d	61.5 (59.7-63.3)	32.1 (30.8-33.4)	59.0 (57.1-60.8)	34.4 (33.1-35.8)	42.9
B <sub>fix</sub> -24w-ABS	46.6 (44.8-48.4)	51.2 (49.8-52.6)	62.3 (60.8-63.8)	35.6 (34.1-37.2)	49.5
B <sub>fix</sub> -48w-90d	72.3 (70.7-74.0)	24.8 (23.6-26.1)	60.5 (58.3-62.6)	36.1 (34.9-37.4)	42.4
B <sub>fix</sub> -48w-180d	61.5 (59.7-63.3)	32.1 (30.8-33.4)	58.7 (56.8-60.6)	34.7 (33.4-36.0)	43.0
B <sub>fix</sub> -48w-ABS	46.6 (44.8-48.4)	51.8 (50.4-53.2)	62.3 (60.8-63.8)	36.2 (34.6-37.8)	49.9
B <sub>fix</sub> -Sust-90d	74.1 (72.3-75.8)	20.4 (19.0-21.8)	50.9 (48.2-53.7)	41.4 (39.9-42.8)	43.5
B <sub>fix</sub> -Sust-180d	63.8 (61.9-65.7)	27.4 (25.9-29.0)	50.0 (47.7-52.3)	40.0 (38.5-41.6)	43.1
B <sub>fix</sub> -Sust-ABS	47.7 (45.7-49.7)	49.1 (47.3-50.8)	55.3 (53.5-57.1)	41.5 (39.7-43.4)	48.5
B <sub>rov</sub> -24w-90d	72.3 (70.7-74.0)	22.5 (21.4-23.5)	63.1 (61.0-65.1)	30.7 (29.6-31.8)	38.5
B <sub>rov</sub> -24w-180d	61.5 (59.7-63.3)	30.2 (29.0-31.3)	62.3 (60.5-64.0)	29.5 (28.3-30.7)	40.3
B <sub>rov</sub> -24w-ABS	46.6 (44.8-48.4)	48.7 (47.4-50.0)	65.8 (64.4-67.2)	30.1 (28.8-31.5)	48.0
B <sub>rov</sub> -48w-90d	72.3 (70.7-74.0)	23.6 (22.5-24.7)	64.0 (62.0-66.0)	31.2 (30.1-32.3)	39.4
B <sub>rov</sub> -48w-180d	61.5 (59.7-63.3)	30.2 (29.0-31.4)	62.1 (60.3-63.8)	29.7 (28.5-30.9)	40.3
B <sub>rov</sub> -48w-ABS	46.6 (44.8-48.4)	49.5 (48.3-50.8)	65.9 (64.5-67.3)	30.7 (29.3-32.1)	48.6
B <sub>rov</sub> -Sust-90d	74.2 (72.4-75.9)	19.3 (18.1-20.5)	54.7 (52.0-57.3)	36.3 (34.9-37.6)	40.3
B <sub>rov</sub> -Sust-180d	63.9 (62.0-65.8)	26.0 (24.6-27.4)	53.8 (51.5-56.0)	34.8 (33.4-36.2)	40.5
B <sub>rov</sub> -Sust-ABS	47.7 (45.5-49.7)	46.7 (45.1-48.3)	59.1 (57.3-60.8)	35.7 (34.0-37.3)	47.1

## Legend to eTable 5

EDSS: Expanded Disability Status Scale, NPV: Negative Predictive Value; PPV: Positive Predictive Value; B<sub>fix</sub>: fixed baseline; B<sub>rov</sub>: roving baseline; 24w: 24-week confirmation; 48w: 48-week confirmation; Sust: sustained disability accrual; 90d: no relapses  $\leq$  90 days before and  $\leq$  30 days after the event score; 180d: no relapses  $\leq$  180 days before and  $\leq$  30 days after the event score; ABS: no relapses from baseline to the confirmation score