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The Effects of Daclizumab High-Yield Process (DAC HYP) on Patient-Centered Functional Outcomes: Results From the DECIDE Study

Michael Kaufman, MD

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Michael Kaufman, MD,¹ Ludwig Kappos, MD,² Krzysztof Selmaj, MD,³ Douglas Arnold, MD,^{4,5} Eva Havrdova, MD,⁶ Alexey Boyko, MD,⁷ Heinz Wiendl, MD,⁸ John Rose, MD,⁹ Steven Greenberg, MD,¹⁰ Wei Ma, PhD,¹¹ Ping Wang, PhD,¹¹ Lou Barbato, MD¹¹

¹Cole Neurological Institute, University of Tennessee, Knoxville, TN, USA; ²University Hospital Basel, Basel, Switzerland; ³Medical University of Lodz, Lodz, Poland; ⁴McGill University, Montreal, Canada; ⁵NeuroRx Research, Montreal, Canada; ⁶First Faculty of Medicine, Charles University in Prague, Prague, Czech Republic; ⁷Russian National Research Medical University named after N.I. Pirogov and the Moscow Multiple Sclerosis Center, Moscow, Russia; ⁸University of Münster, Münster, Germany; ⁹Department of Neurology, University of Utah and Neurovirology Research Laboratory VASLCHCS, Imaging and Neuroscience Center, Salt Lake City, UT, USA; ¹⁰AbbVie Biotherapeutics Inc., Redwood City, CA, USA; ¹¹Biogen, Cambridge, MA, USA

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Introduction

- Ambulation and cognition are priorities for patients with multiple sclerosis (MS)
- The randomized, double-blind DECIDE study found daclizumab high-yield process (DAC HYP) 150 mg subcutaneous (SC) reduced clinical and radiographic disease activity in patients with relapsing-remitting MS (RRMS) compared with interferon (IFN) beta-1a 30 mcg intramuscular (IM)¹
 - DAC HYP was associated with elevated risk of infections, cutaneous adverse events, and hepatic enzyme abnormalities¹

1. Kappos L, et al. Daclizumab HYP versus interferon beta-1a in relapsing-remitting multiple sclerosis: Primary results of the DECIDE study. Presented at: 67th Annual Meeting of the American Academy of Neurology; April 18-25, 2015; Washington, DC.

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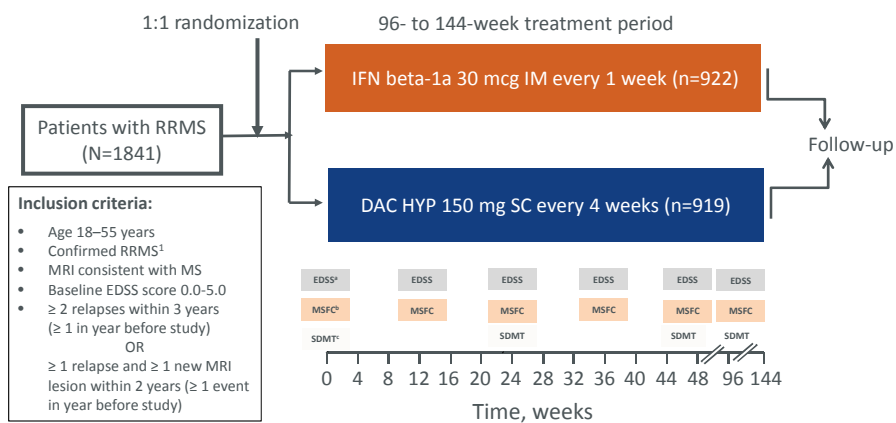
Objective

- To evaluate the effects of DAC HYP vs. IM IFN beta-1a on ambulation, hand/arm dexterity, and cognition, using the Multiple Sclerosis Functional Composite (MSFC) and Symbol Digit Modalities Test (SDMT) in DECIDE

1. Kappos L, et al. Daclizumab HYP versus interferon beta-1a in relapsing-remitting multiple sclerosis: Primary results of the DECIDE study. Presented at: 67th Annual Meeting of the American Academy of Neurology; April 18-25, 2015; Washington, DC.

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DECIDE Study Design Overview



- Changes in MSFC and SDMT were included as tertiary endpoints in DECIDE

EDSS = Expanded Disability Status Scale; MRI = magnetic resonance imaging. ^aAlso assessed at Weeks 60, 72, 84, 108, 120, 132, and 144. ^bAlso assessed at Weeks 60, 72, 84, 120, 132, and 144. ^cAlso assessed at Weeks 72, 120, and 144. 1. Polman CH, et al. *Ann Neurol*. 2005;58(6):840-846.

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Demographics and Baseline Characteristics

Characteristic	IFN beta-1a 30 mcg IM n=922	DAC HYP 150 mg SC n=919
Mean (SD) age, y	36.2 (9.3)	36.4 (9.4)
Female, n (%)	627 (68)	625 (68)
Mean (SD) duration of disease, y ^a	4.1 (4.7)	4.2 (5.0)
Mean (SD) relapses within previous year	1.6 (0.8)	1.5 (0.7)
Mean (SD) EDSS score	2.5 (1.3)	2.5 (1.2)
Previous DMT, n (%) ^b	376 (41)	380 (41)
Mean (SD) no. of Gd ⁺ lesions	2.3 (5.9) n=909	2.0 (5.9) n=900
No. with any Gd ⁺ lesion, n (%)	414 (45)	398 (43)
Mean (SD) no. of T2 lesions	51.8 (37.4) n=908	49.2 (35.5) n=900

DMT = disease-modifying therapy; Gd⁺ = gadolinium-enhancing. ^aTime since MS diagnosis. ^bIncludes IFN beta, glatiramer acetate, natalizumab, mitoxantrone, azathioprine, fumaric acid, laquinimod, cyclophosphamide, mycophenolic acid, fingolimod, teriflunomide, methotrexate, alemtuzumab, cladribine, immunoglobulins, tamsulosin.

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Multiple Sclerosis Functional Composite (MSFC)^a

Timed 25-Foot Walk (T25FW)

- Assesses ambulatory function
- Time to walk 25 feet → time increase of $\geq 20\%$ meaningful

9-Hole Peg Test (9-HPT)

- Measures arm and hand function
- Time to insert and remove 9 pegs first with dominant hand and then with nondominant hand → mean time for both hands

3-Second Paced Auditory Serial Addition Test (PASAT-3)

- Measures cognition function
- Patient listens to a series of 61 spoken numbers separated by 3-second intervals, and each number must be added to the previous number → number of correct additions

^aDeveloped by the National Multiple Sclerosis Society Clinical Outcomes Assessment Task Force, 1997. Polman CH, Rudick RA. *Neurology*. 2010;74(suppl 3):S8-S15.

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MSFC: A Measure of Disability in MS

- Summary of the 3 MSFC components (T25FW, 9-HPT, and PASAT-3):

MSFC Component	Unit of Measure	Indicates Deterioration
T25FW	Time (s)	Higher Score
9-HPT	Time (s)	Higher Score
PASAT-3	Number Correct	Lower Score

- Generate appropriately weighted composite using the z score
 - z scores are the number of standard deviations between scores for the individual and the reference population (e.g., MS population)
 - Negative change in MSFC z scores compared with Baseline or prior measurements indicate neurologic deterioration and disability progression, while a positive change in z score indicates neurologic improvement

Polman CH, Rudick RA. *Neurology*. 2010;74(suppl 3):S8-S15.

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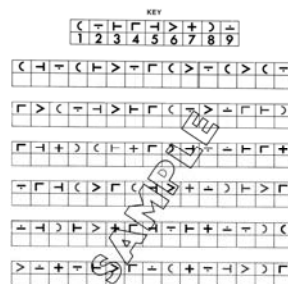
Symbol Digit Modalities Test (SDMT)

Outcome Measures

- Measure of cognition (not part of the MSFC)
- Quickly screens for cerebral dysfunction in children 8 years and older and adults

Scoring

- Takes < 5 minutes
- Patient substitutes a number, either orally or written, for randomized presentations of geometric figures that are defined in a key



Smith A. *Symbol Digit Modalities Test Manual*. Torrance, CA: Western Psychological Services; 1973.

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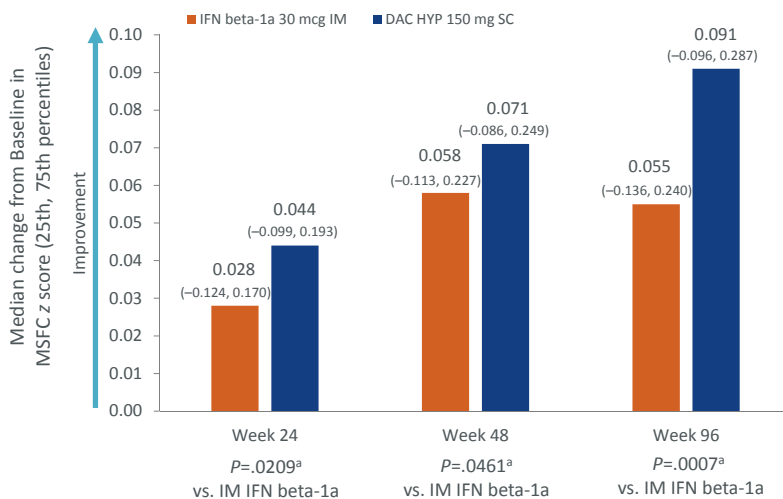
MSFC and SDMT Scores at Baseline

	IFN beta-1a 30 mcg IM n=922	DAC HYP 150 mg SC n=919
Median MSFC z score (25th, 75th percentiles)	0.118 (-0.377, 0.482) n=920	0.139 (-0.335, 0.491) n=916
Median T25FW z score (25th, 75th percentiles)	0.223 (-0.042, 0.372)	0.223 (-0.034, 0.372)
Median 9-HPT z score (25th, 75th percentiles)	0.035 (-0.622, 0.633)	0.065 (-0.597, 0.661)
Median PASAT-3 z score (25th, 75th percentiles)	0.264 (-0.619, 0.794)	0.352 (-0.531, 0.794)
Mean (SD) SDMT score	47.66 (16.08) n=880	48.53 (15.92) n=884

z scores were calculated based on a reference population mean of 6.896 and SD of 6.034 for the T25FW; a mean of 0.047 and SD of 0.011 for the 9-HPT; and a mean of 47.011 and SD of 11.321 for the PASAT-3. Observed data after patients switched to alternative MS medications were excluded. Missing values were imputed.

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Median Change From Baseline in MSFC z Score at Weeks 24, 48, and 96



^aP value for comparison between the DAC HYP and IFN beta-1a groups was based on an analysis of covariance model based on ranks and adjusted for the baseline z score, baseline age (≤ 35 , > 35 years), and prior IFN beta use. Missing values were imputed.

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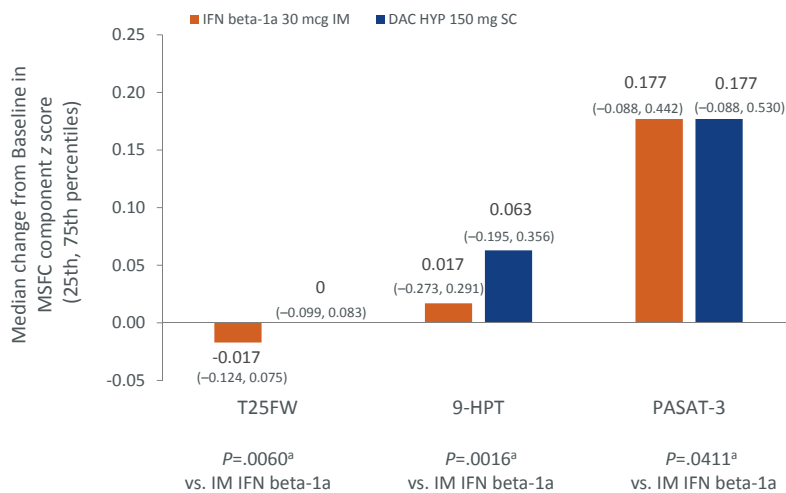
Change From Baseline to Week 96 in MSFC Component z Scores

Component	IFN beta-1a 30 mcg IM n=922	DAC HYP 150 mg SC n=919	P value vs. IFN beta-1a ^a
Median T25FW z score (25th, 75th percentiles)	-0.017 (-0.124, 0.075)	0.000 (-0.099, 0.083)	.0060
Median 9-HPT z score (25th, 75th percentiles)	0.017 (-0.273, 0.291)	0.063 (-0.195, 0.356)	.0016
Median PASAT-3 z score (25th, 75th percentiles)	0.177 (-0.088, 0.442)	0.177 (-0.088, 0.530)	.0411

^aP value for comparison between the DAC HYP and IFN beta-1a groups was based on an analysis of covariance model based on ranks and adjusted for the baseline z score, baseline age (≤ 35 , > 35 years), and prior IFN beta use. Missing values were imputed.

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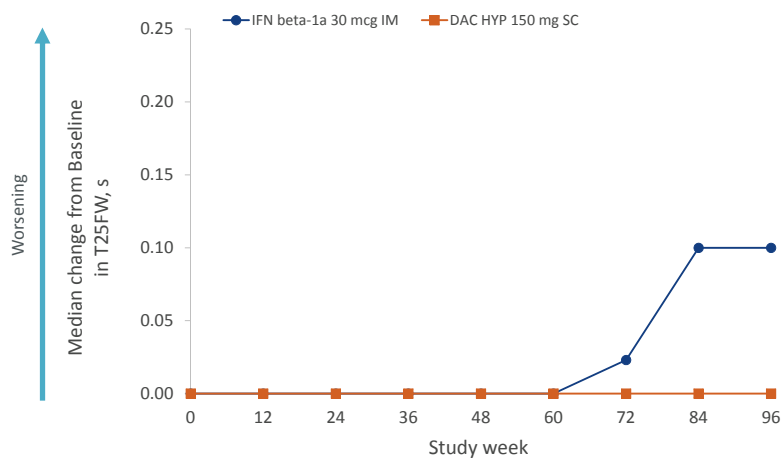
Change From Baseline to Week 96 in MSFC Component z Scores



^aP value for comparison between the DAC HYP and IFN beta-1a groups was based on an analysis of covariance model based on ranks and adjusted for the baseline z score, baseline age (≤ 35 , > 35 years), and prior IFN beta use. Missing values were imputed.

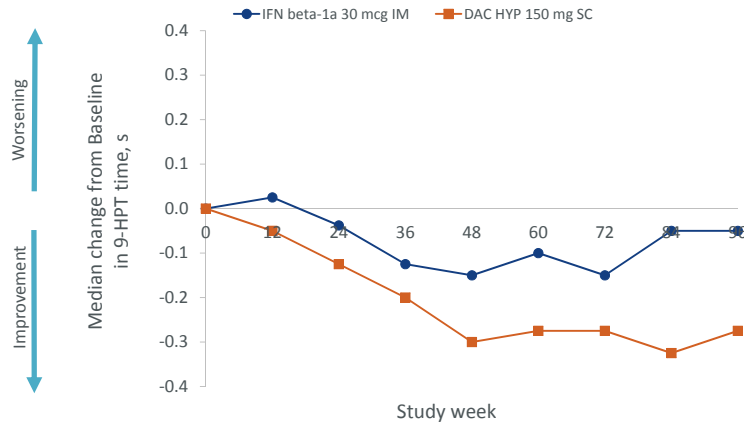
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Median Change from Baseline in T25FW time



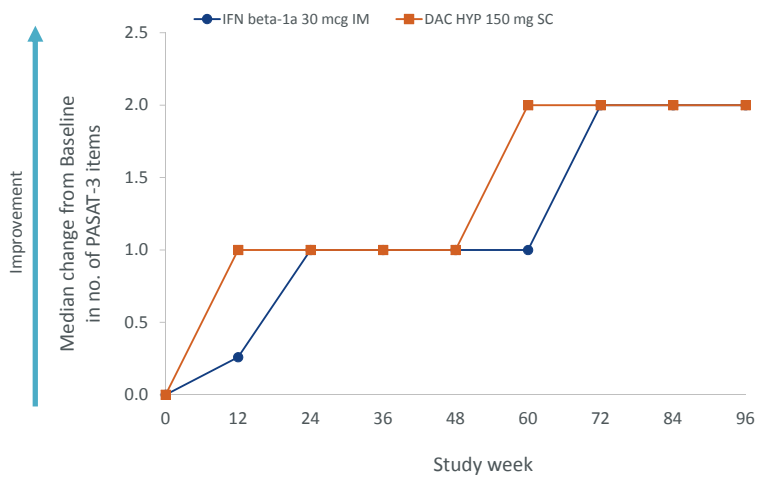
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Median Change From Baseline in 9-HPT



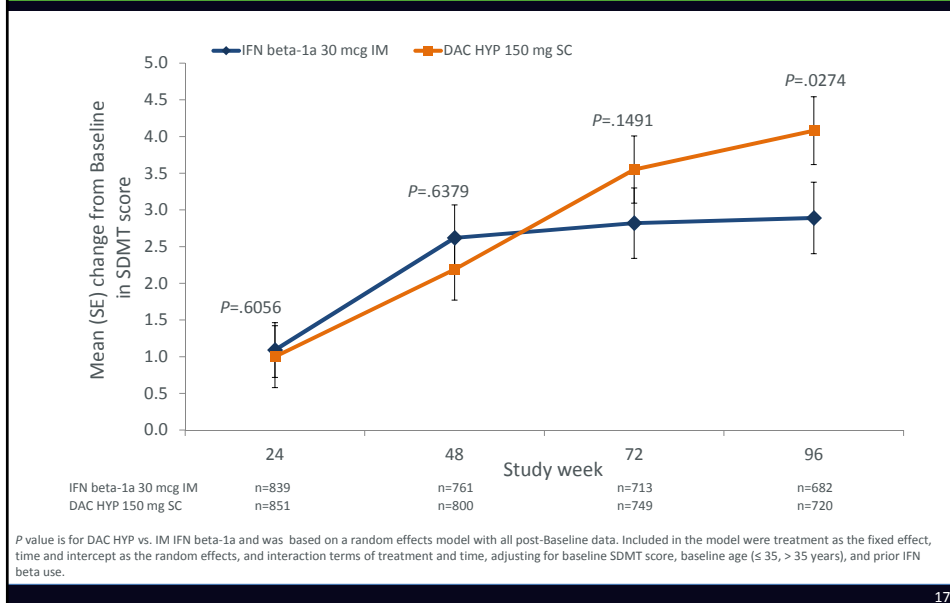
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Median Change From Baseline in Number of PASAT-3 Items



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Mean (SE) Change From Baseline in SDMT Score



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Conclusions

- Over 2–3 years of treatment, DAC HYP showed greater improvement compared with IM IFN beta-1a on patient-centered measures of functional disability
 - Improvement on MSFC composite z score ($P=.0007$) and all z scores of all subcomponents ($P<.05$)
 - Improvement on SDMT ($P=.0274$)
- The findings of these objective measures of function and cognition support the findings that DAC HYP demonstrated superior efficacy to IM IFN beta-1a across key clinical and radiographic MS outcome measures¹
- DAC HYP has the potential to be a new treatment option for patients with RRMS

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BACK UP

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Median Change From Baseline to Weeks 24, 48, and 96 in T25FW^a

Study visit	IFN beta-1a 30 mcg IM n=922	DAC HYP 150 mg n=919
Median change at Week 24 (25th, 75th percentiles), s	0.000 (-0.350, 0.500)	0.000 (-0.400, 0.400)
Median change at Week 48 (25th, 75th percentiles), s	0.000 (-0.450, 0.500)	0.000 (-0.500, 0.450)
Median change at Week 96 (25th, 75th percentiles), s	0.100 (-0.450, 0.750)	0.000 (-0.500, 0.600)

^aIncrease in time indicates worsening.

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T25FW z Score: Change From Baseline to Weeks 24, 48, and 96

Study visit	IFN beta-1a 30 mcg IM n=922	DAC HYP 150 mg SC n=919	P value vs. IFN beta-1a ^a
Median change at Week 24 (25th, 75th percentiles)	0.000 (-0.083, 0.058)	0.000 (-0.066, 0.066)	.1299
Median change at Week 48 (25th, 75th percentiles)	0.000 (-0.083, 0.075)	0.000 (-0.075, 0.083)	.0894
Median change at Week 96 (25th, 75th percentiles)	-0.017 (-0.124, 0.075)	0.000 (-0.099, 0.083)	.0060

z scores were calculated based on a reference population mean of 6.896 and SD of 6.034 for the T25FW; a mean of 0.047 and SD of 0.011 for the 9-HPT; and a mean of 47.011 and SD of 11.321 for the PASAT-3. Observed data after patients switched to alternative MS medications are excluded. Missing data up to Week 96 are imputed as described in the statistical analysis plan. ^aP value for comparison between the DAC HYP and IFN beta-1a groups was based on an analysis of covariance model based on ranks and adjusted for baseline z score, baseline age (≤ 35 , > 35 years), and prior IFN beta use.

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9-HPT z Score: Change From Baseline to Weeks 24, 48, and 96

Study visit	IFN beta-1a 30 mcg IM n=922	DAC HYP 150 mg SC n=919	P value vs. IFN beta-1a ^a
Median change at Week 24 (25th, 75th percentiles)	0.001 (-0.213, 0.228)	0.025 (-0.178, 0.260)	.1010
Median change at Week 48 (25th, 75th percentiles)	0.031 (-0.218, 0.285)	0.063 (-0.180, 0.317)	.0756
Median change at Week 96 (25th, 75th percentiles)	0.017 (-0.273, 0.291)	0.063 (-0.195, 0.356)	.0016

^aP value based on an analysis of covariance model based on ranks and adjusted for baseline z score, baseline age (≤ 35 , > 35 years), and prior IFN beta use. Missing values were imputed.

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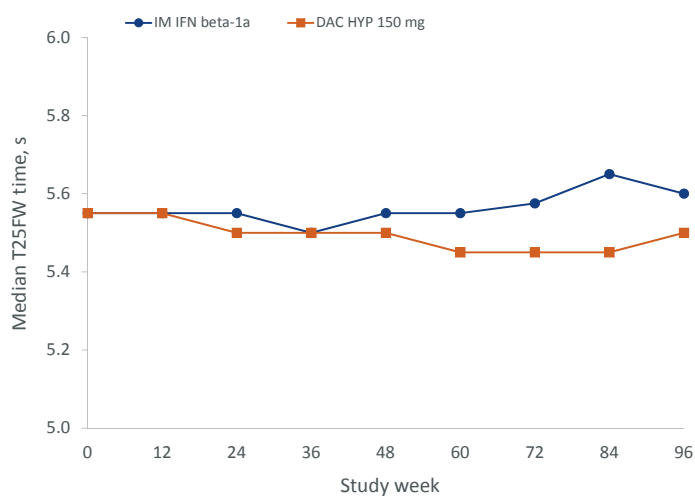
PASAT-3 z Score: Change From Baseline to Weeks 24, 48, and 96

Study visit	IFN beta-1a 30 mcg IM n=922	DAC HYP 150 mg SC n=919	P value vs. IFN beta-1a ^a
Median change at Week 24 (25th, 75th percentiles)	0.088 (-0.177, 0.353)	0.088 (-0.177, 0.353)	.3238
Median change at Week 48 (25th, 75th percentiles)	0.088 (-0.088, 0.442)	0.088 (-0.177, 0.442)	.3177
Median change at Week 96 (25th, 75th percentiles)	0.177 (-0.088, 0.442)	0.177 (-0.088, 0.530)	.0411

^aP value based on an analysis of covariance model based on ranks and adjusted for baseline z score, baseline age (≤ 35 , > 35 years), and prior IFN beta use. Missing values were imputed.

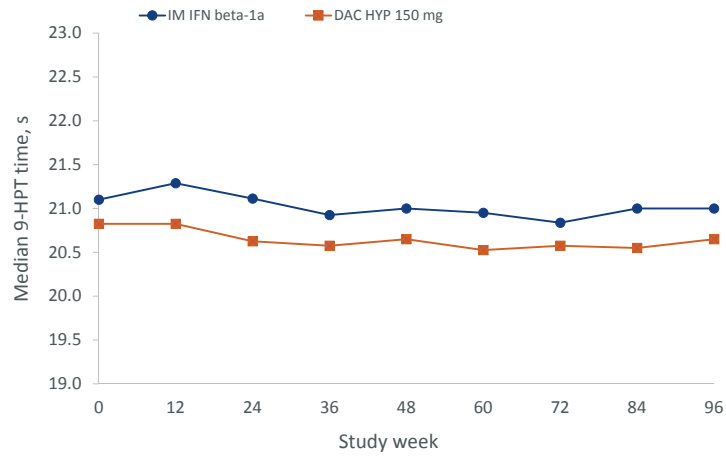
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Median T25FW Score



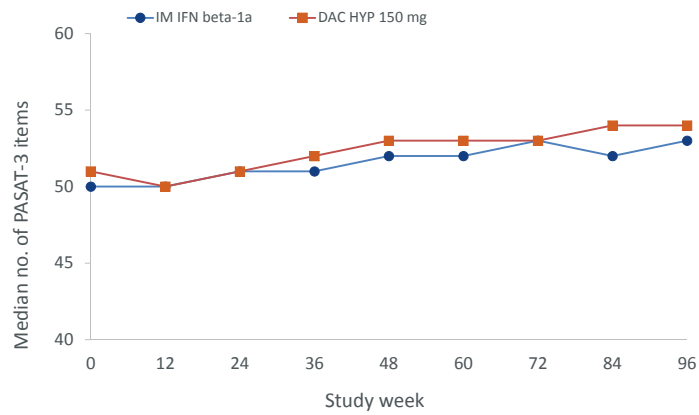
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Median 9-HPT Time



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Median Number of PASAT-3 Items



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