

# Employment and Cognitive Improvements in Ocrelizumab-Treated Patients with Relapsing-Remitting Multiple Sclerosis: 96-Week CASTING Study Data

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## BACKGROUND

- Multiple sclerosis (MS) affects mainly adults of working age, impacting employment<sup>1-3</sup> and quality of life (QoL)<sup>4</sup>
- Cognitive impairment is a key symptom in people with MS (PwMS) and is associated with unemployment and lower QoL<sup>5</sup>
  - The Symbol Digit Modalities Test (SDMT) measures cognitive processing speed

- Employment enhances QoL and is a gauge of overall functioning in PwMS<sup>6</sup>
  - The Work Productivity and Activity Impairment (WPAI) questionnaire is a patient-reported outcome assessing percentage work time missed (absenteeism), impairment while working (presenteeism), overall work impairment (work productivity) and activity impairment, in the preceding 7 days

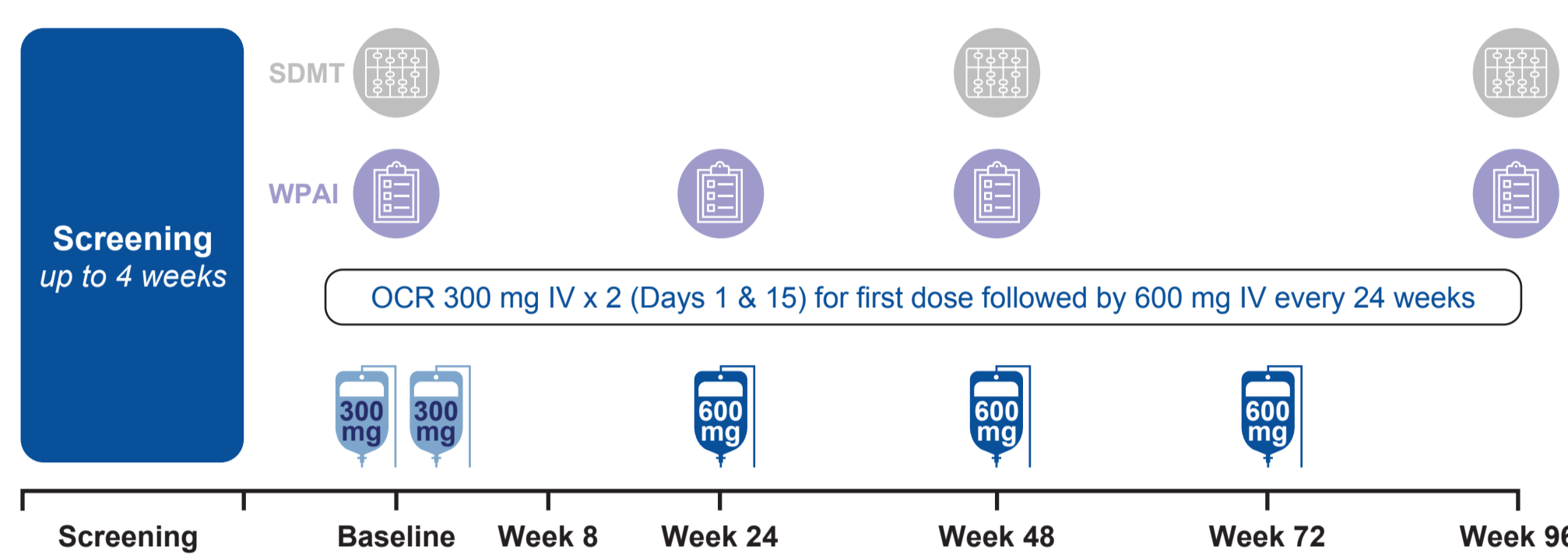
Ensuring work participation and reduced cognitive impairment in PwMS is beneficial to both those with MS and society

To report employment status by baseline demographic, disease history and cognitive function, and changes in employment status over 96 weeks, in patients with relapsing-remitting MS (RRMS) who switched from a prior disease-modifying therapy (DMT) to ocrelizumab in the Phase IIIb CASTING trial (NCT02861014)

## METHODS

### CASTING Study Design

CASTING patients received IV OCR 600 mg every 24 weeks for 96 weeks



Patients (18-55 years) with a diagnosis of RRMS and a suboptimal response to one or two previous DMTs

Disease duration from first symptom <10 years

EDSS score at screening of 0.0-4.0

Treated with a DMT for at least 6 months and with suboptimal efficacy within the last 12 months whilst on the DMT

Unemployment status, derived from the WPAI questionnaire, was assessed in relation to SDMT and EDSS score

DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; IV, intravenous; OCR, ocrelizumab; RRMS, relapsing-remitting multiple sclerosis; SDMT, Symbol Digit Modalities Test; WPAI, Work Productivity and Activity Impairment.

### Work Productivity and Activity Impairment (WPAI)

- WPAI questionnaire was used to determine employment status at baseline, Weeks 24, 48 and 96
- Baseline demographics and disease characteristics were categorised according to baseline employment status, i.e.
  - Employed
  - Unemployed

### WPAI Questionnaire<sup>7</sup>

### Symbol Digit Modalities Test (SDMT)<sup>8</sup>

- The SDMT<sup>8</sup> used to measure cognitive processing speed, was assessed at baseline, Weeks 48 and 96
  - SDMT scores were also translated to z-scores
    - The z-score gives an idea of how far from the mean a data point is<sup>9</sup>
      - It describes the position of an original (raw) score in terms of its distance from the mean, when measured in standard deviation units
      - z-scores lie in the range of -3 to +3 on a normal distribution curve
  - SDMT scores were translated to z-scores (derived using published norms<sup>10</sup>), with a cut-off of -1 to define high and low SDMT score groups<sup>11</sup>
    - Baseline z-score ≤ -1 defined the lower cognitive functioning subgroup
    - Baseline z-score > -1 defined the higher cognitive functioning subgroup

In the SDMT, patients are required to substitute digits for symbols from a reference key.

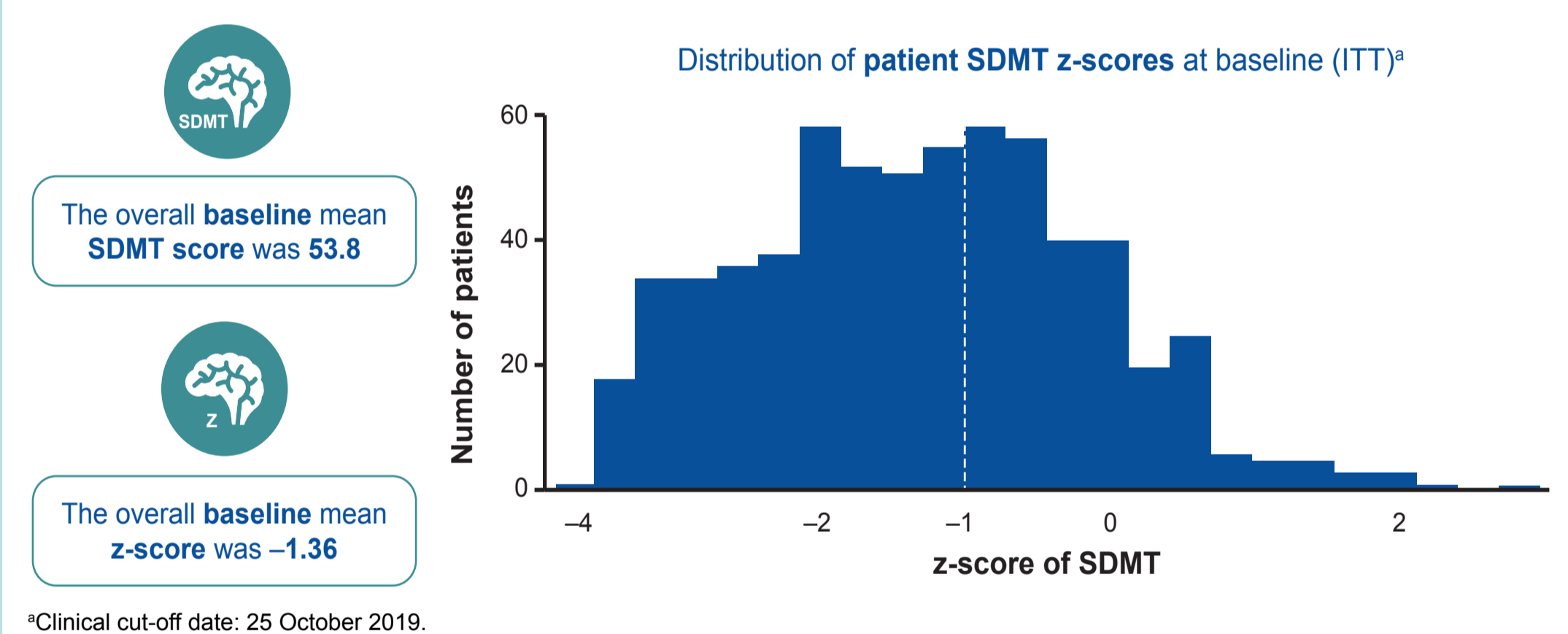
\*NB: In the congress Abstract, the subgroup with baseline z-score ≤ -1 was defined as cognitively impaired (here defined as 'lower cognitive functioning') and the subgroup with baseline z-score > -1 was defined as minimally impaired (here defined as 'higher cognitive functioning'). \*Alternate forms of SDMT<sup>11</sup> were applied throughout the study to avoid any learning effects.

## RESULTS

### Baseline Employment Status



### Baseline SDMT and z-Score – Overall Population

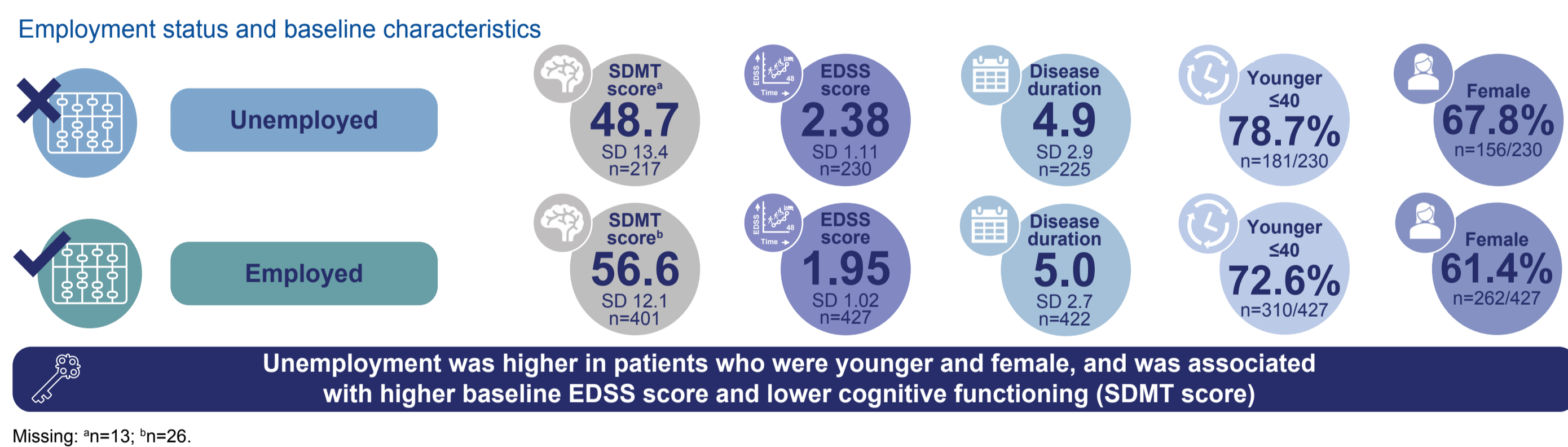


### Baseline Demographic and Disease Characteristics

Parameter	CASTING population (N=680) <sup>a</sup>	Employed (N=427)	Unemployed (N=230)
Mean age (SD), years	34.2 (8.6)	35.1 (8.1)	32.6 (8.2)
Age group, 40-year threshold, n (%)			
≤40	511 (75.1)	310 (72.6)	181 (78.7)
>40	169 (24.9)	117 (27.4)	49 (21.3)
Female, n (%)	436 (64.1)	262 (61.4)	166 (72.6)
Caucasian, n (%) <sup>b</sup>	626 (91.9)	398 (93.2)	205 (89.1)
Weight, kg mean (SD)	72.9 (17.5)	73.2 (17.5)	72.1 (16.9)
BMI, kg/m <sup>2</sup> mean (SD)	25.0 (6.4)	24.9 (6.2)	25.1 (6.5)
Baseline EDSS, mean (SD) <sup>c</sup>	2.1 (1.1)	2.0 (1.0)	2.4 (1.1)
Duration since MS symptom onset, mean (SD), years	5.0 (2.7)	5.0 (2.7)	4.9 (2.9)
Enrolled due to, n (%)			
Only MS relapse	238 (35.0)	150 (35.1)	77 (33.5)
Only MRI relapse <sup>d</sup>	167 (24.6)	109 (25.6)	55 (23.9)
Both relapse and MRI activity	275 (40.4)	168 (39.3)	98 (42.6)

<sup>a</sup>33 patients had missing data up to Week 96, and were therefore not included in the employed and unemployed analyses; <sup>b</sup>Patient is counted in more than one race when multiple races are checked; <sup>c</sup>Screening EDSS if baseline EDSS is not available; <sup>d</sup>Either ≥1 T1 gadolinium-enhancing lesion(s) and/or ≥2 new/enlarging T2 lesions. BMI, body mass index; EDSS, Expanded Disability Status Scale; MRI, magnetic resonance imaging; MS, multiple sclerosis; SD, standard deviation.

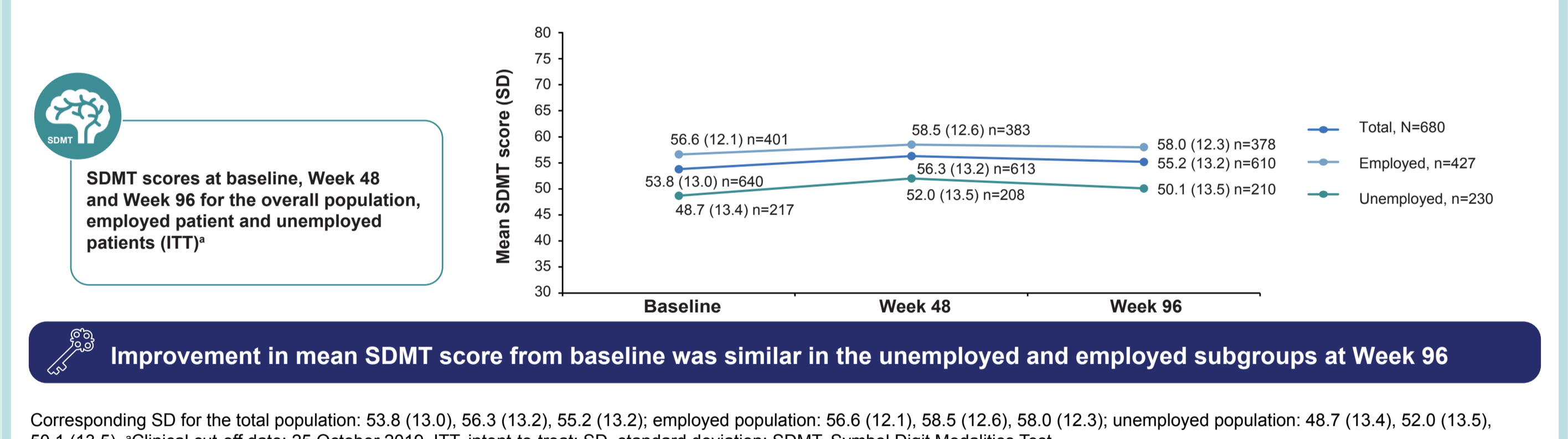
### Characteristics of Unemployed and Employed Subgroups



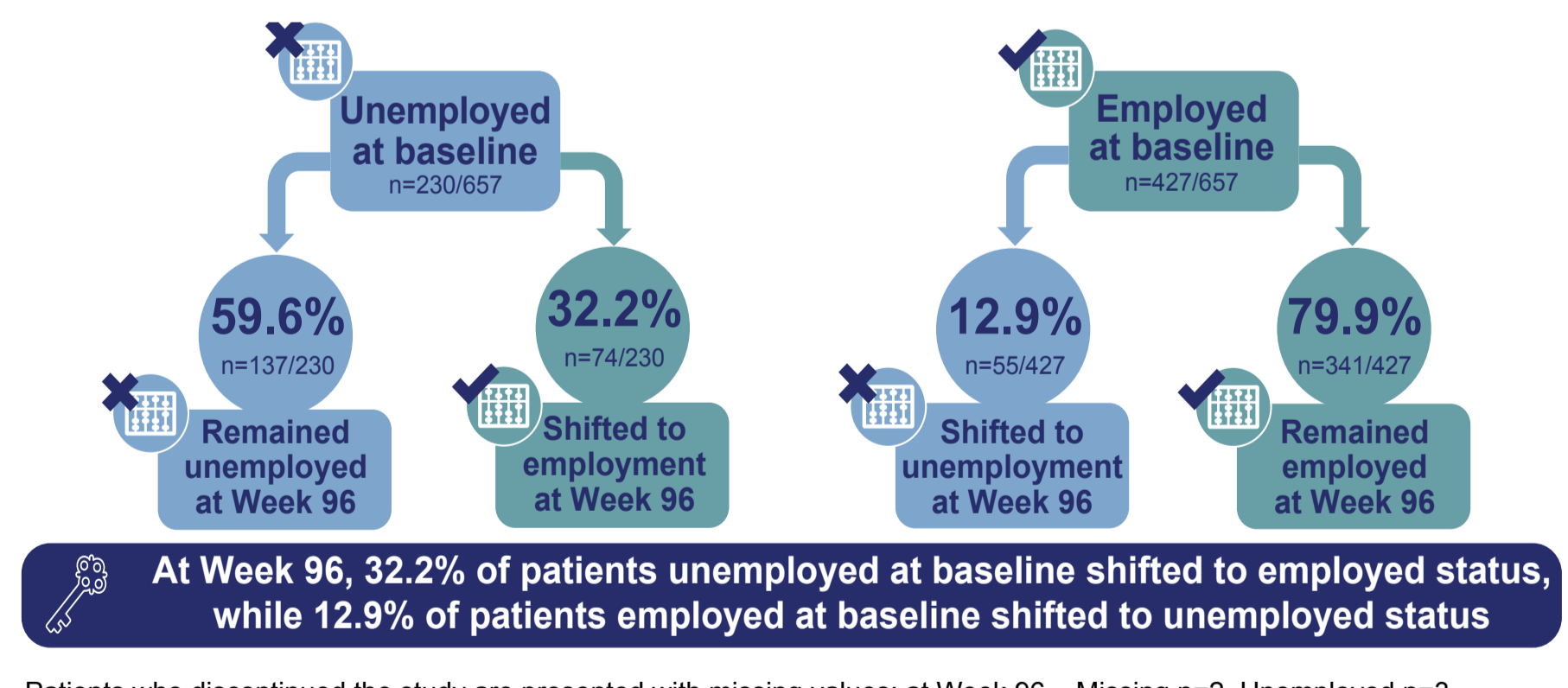
Unemployment was higher in patients who were younger and female, and was associated with higher baseline EDSS score and lower cognitive functioning (SDMT score)

Missing: <sup>a</sup>n=13; <sup>b</sup>n=26. EDSS, Expanded Disability Status Scale; SD, standard deviation; SDMT, Symbol Digit Modalities Test.

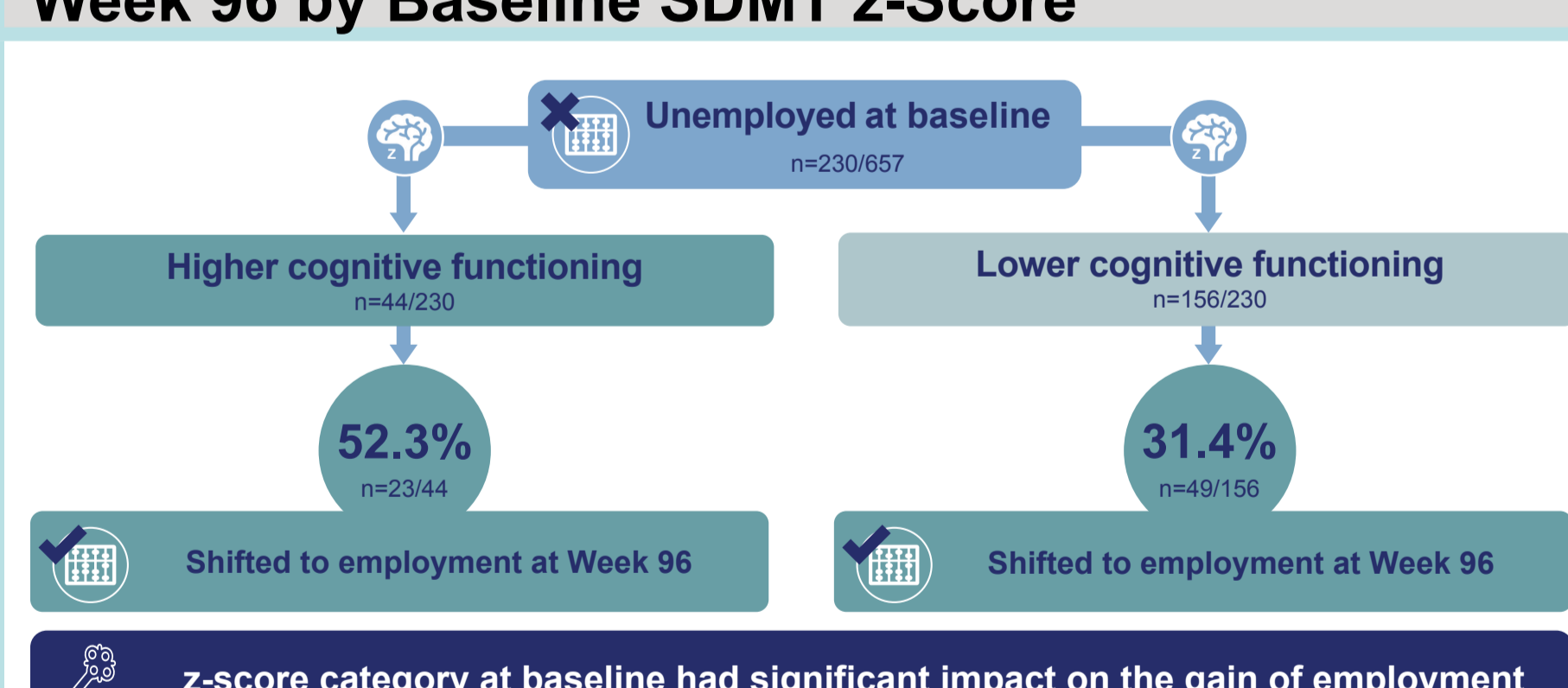
### SDMT Change from Baseline to Week 96 According to Baseline Employment Status



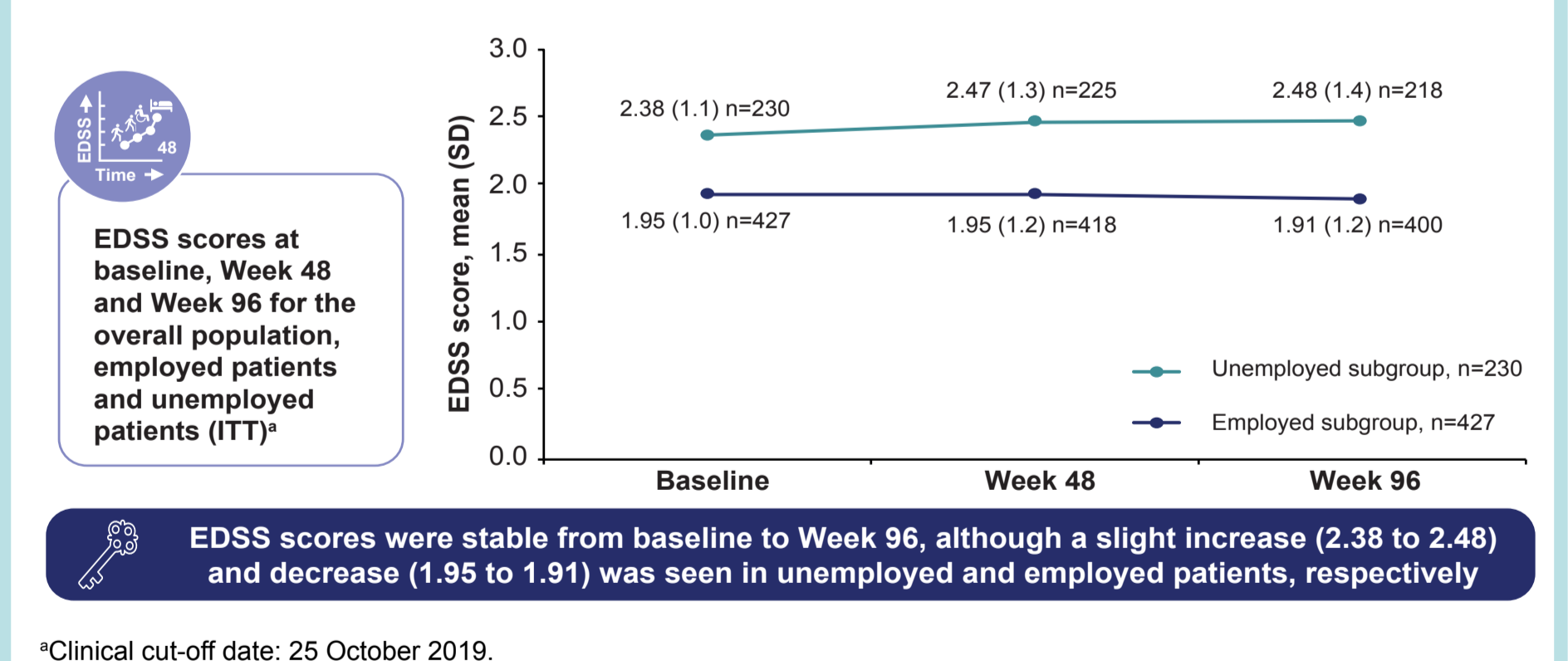
### Shift in Employment Status from Baseline to Week 96



### Shift in Unemployment Status from Baseline to Week 96 by Baseline SDMT z-Score



### EDSS Score Change from Baseline to Week 96



## LIMITATIONS

- A challenge of interpreting the significance of the results is that there is a ceiling effect with the SDMT; many patients did not have impairment at baseline and therefore could not improve, and improvements were driven by the more impaired patients
  - Practice effects are less of an issue with the SDMT as there were 6 months between each assessment and there are alternate forms available<sup>11</sup>
- Baseline characteristics were limited by the population type. Based on the WPAI, 35% of the population was unemployed at baseline; unemployment was higher in younger patients, who were female and was associated with higher baseline EDSS score and lower cognitive functioning

## DISCUSSION

- At baseline, PwMS in the unemployed subgroup had lower SDMT and higher EDSS scores than PwMS in the employed subgroup
  - To ensure there was no learning effect, the definition of the z-score cut-off for the lower cognitively functioning and higher cognitively functioning subgroups differs from the commonly used cut-off of -1.5<sup>12,13</sup>
- The z-score cut-off (-1) was based on the overall population mean z-score (-1.36)

## CONCLUSIONS

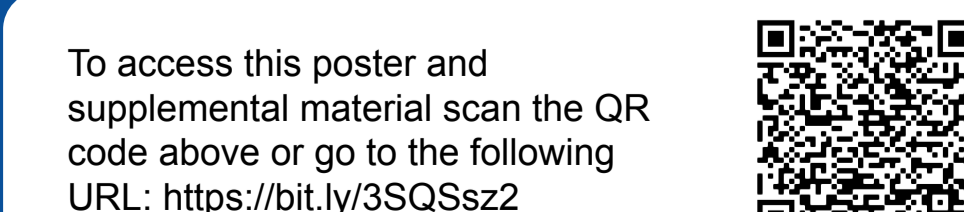
- Unemployment was higher in patients who were younger and female, and was associated with higher baseline EDSS score and lower cognitive functioning
- Over the 2 years of the CASTING study, patients treated with ocrelizumab showed a greater shift towards employment (32.2%) than towards unemployment (12.9%)
  - Prospective data gathered over the same or similar periods in PwMS, largely treated with DMTs, indicated employment status deteriorated between 12.5% to 22.0%<sup>1,14</sup>

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## DISCLOSURES

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