

# Zavesca (miglustat) Saccadic Eye Movements in patients with Neimann-Pick Type C

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# Efficacy Study OGT 918-007

- Randomized (2:1)
- Two centers (Manchester, New York)
- Parallel Group (miglustat vs no treatment)
- Open label
- 2 year study with randomized treatment only during the first year

# Primary Efficacy Endpoint

- HSEM- $\alpha$ 
  - Horizontal Saccadic Eye Movement

- Patients were seated with their head in a chin cup at a distance of 50–100 cm from the targets (light emitting diodes [LEDs] or displayed spots).
- Saccadic eye movement was assessed using video-based techniques.
- Patients were asked not to inform the assessor as to which treatment arm they were randomized.

# Saccade



- Saccade = rapid eye movement
  - usually under voluntary control
- Used to focus from one object to another
- Both eyes usually move together.

# Timing of Evaluations

- Measured at:
  - Screening
  - Month 12
  - Month 24
  - Withdrawal/follow-up visit
    - if not carried out at Month 12.
- Two assessments were performed at each time point, separated by a break of at least 1 hour.

# Horizontal saccades

- Pseudorandom presentation
- Target jumps of
  - 2.5, 5, 7.5, 10, 12.5, 15, 17.5, 20, 25 and 30°
- Distributed across a vertical range of  $\pm 15^\circ$ .

- The time between target jumps was varied to avoid anticipatory responses.
- Both eyes allowed to view the target
  - unless there was a reason to occlude one eye (e.g., diplopia or strabismus).
- Forty-five (45) or more saccades of various amplitudes were used.

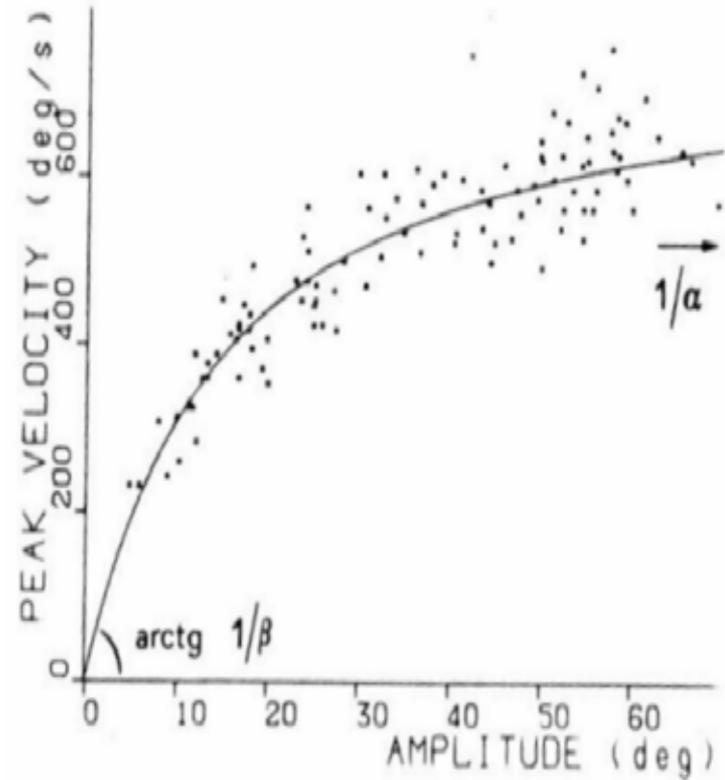
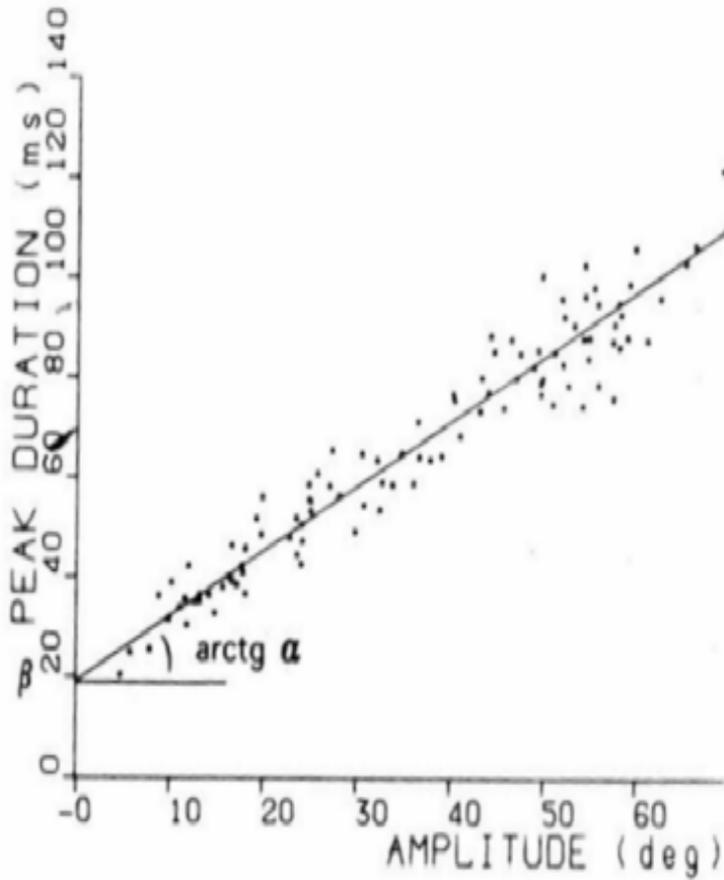
# Different Methods

- Center 1 (Manchester) an infrared system was used to measure eye movements.
- Center 2 (New York) a scleral search coil was used.

- Measure time in milliseconds (ms) to fixate on target
- Plot time (ms) or speed (distance/time) vs distance (degrees)

$\alpha$  = Slope (ms/deg),  $\beta$  = intercept (ms)

- $\beta$  can be thought of as a baseline speed
- $\alpha$  is the additional speed needed to move a farther distance from the center
- Ordinary least squares fit used to draw regression lines

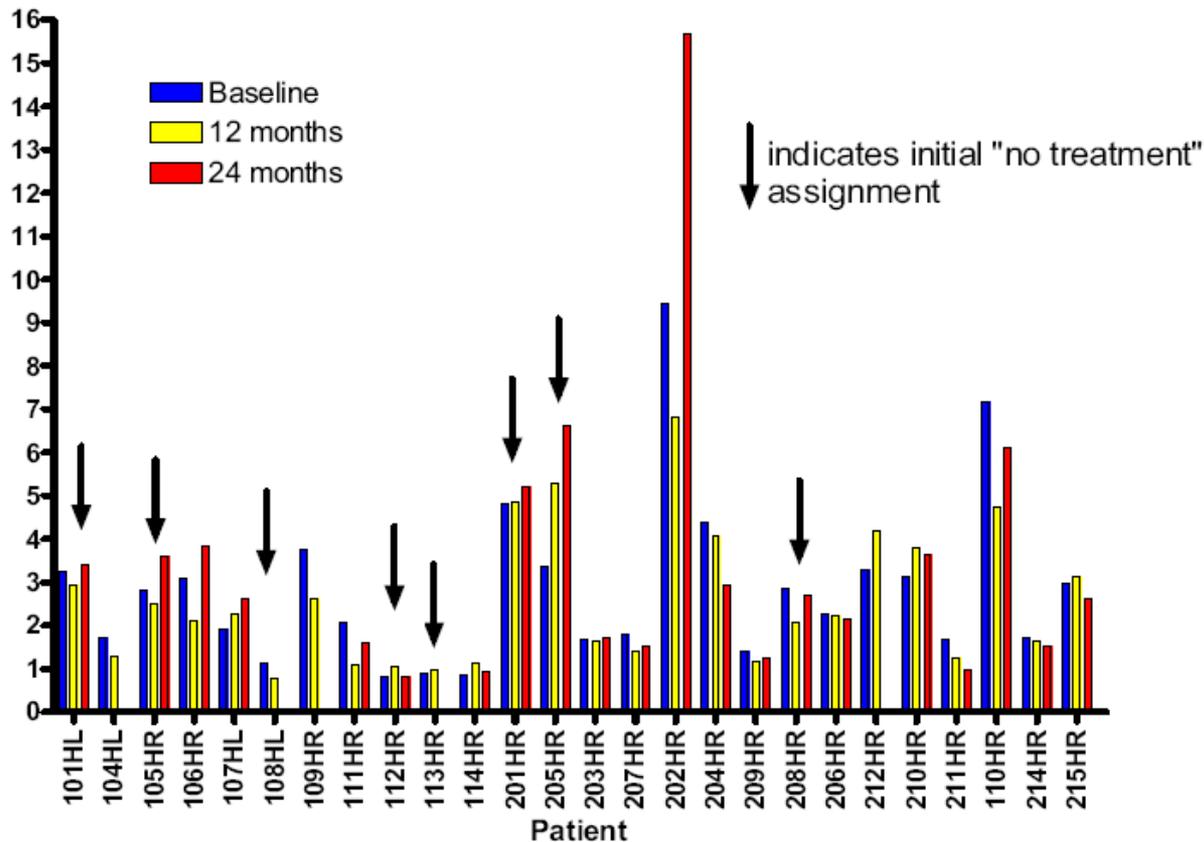


(b)

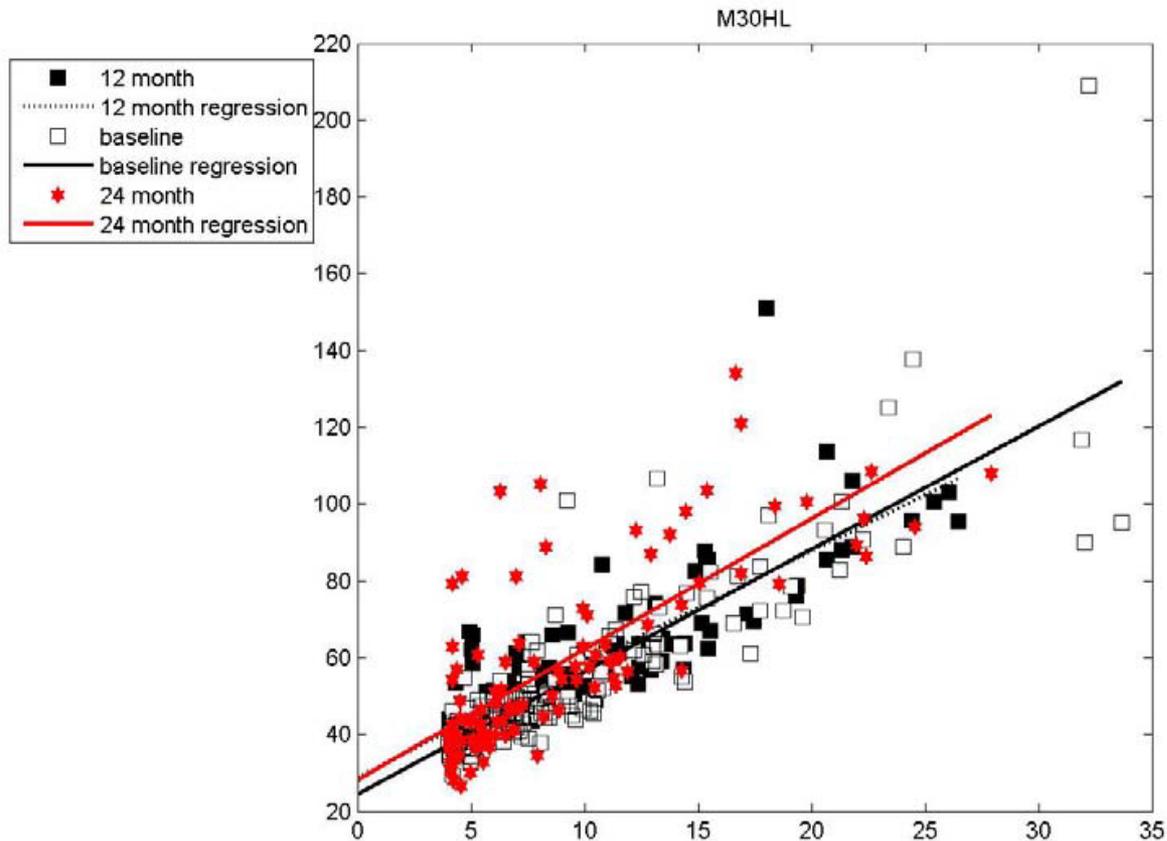
# Summary of Individual Patients (decrease in score = improvement)

Response is variable from patient to patient

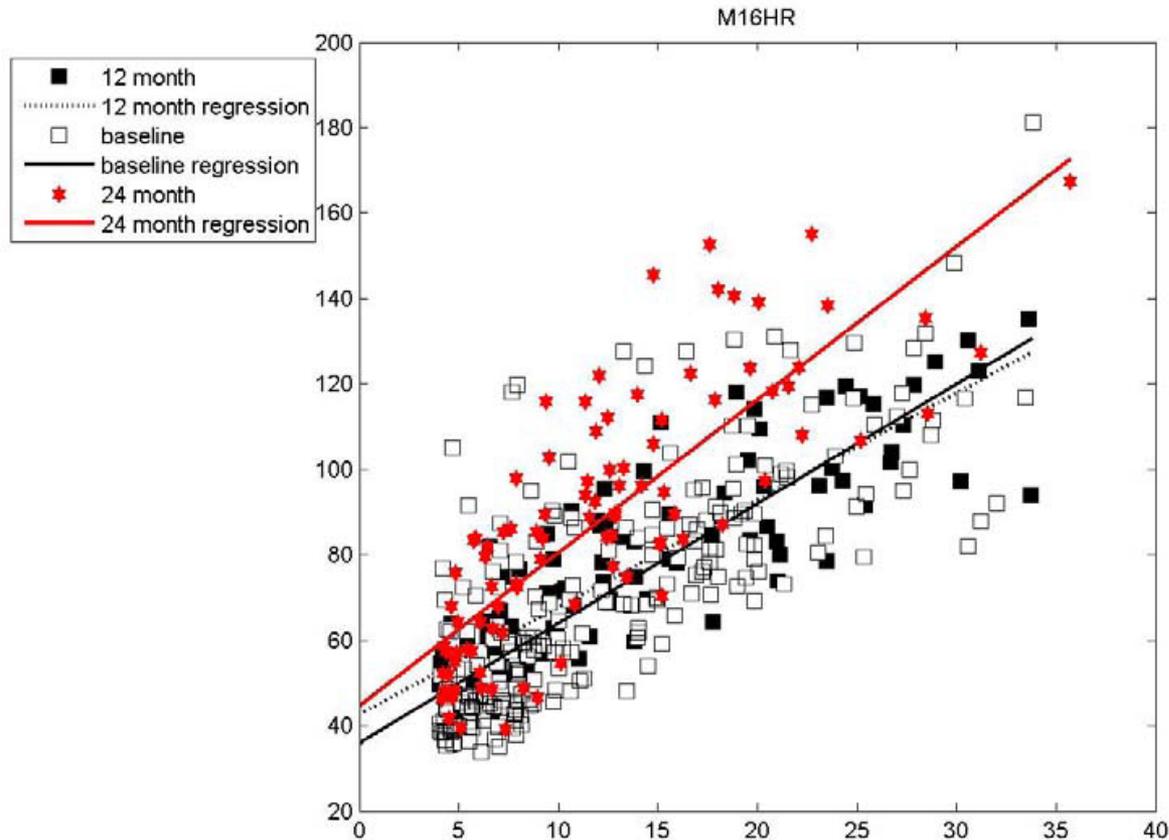
Slopes, NPC data, baseline, 12 and 24 month recordings



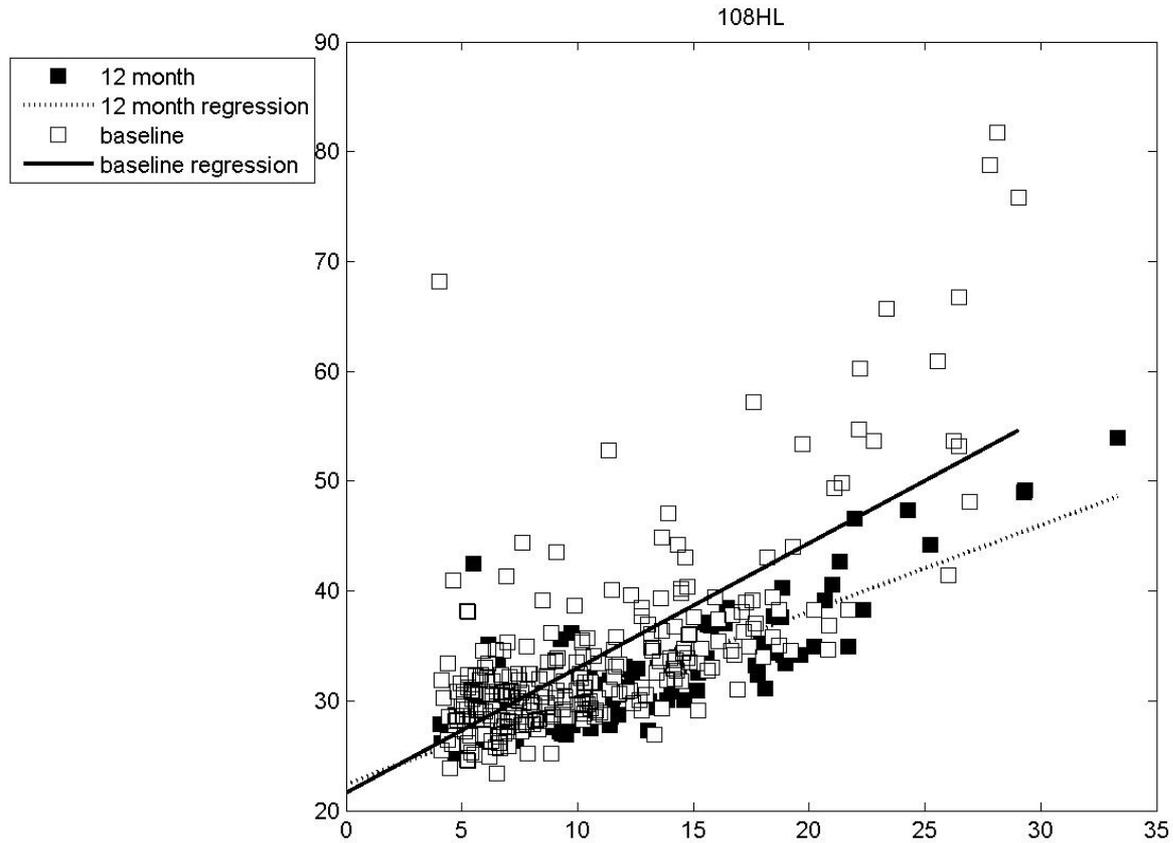
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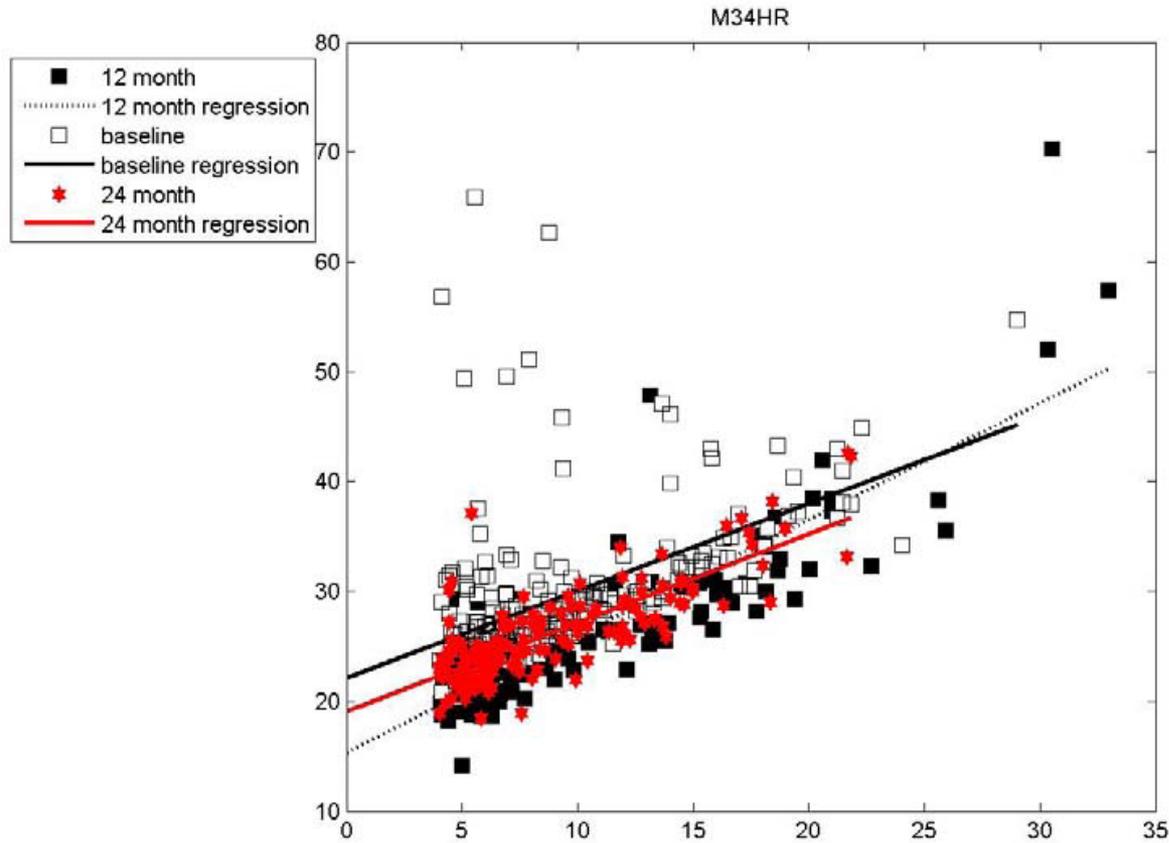
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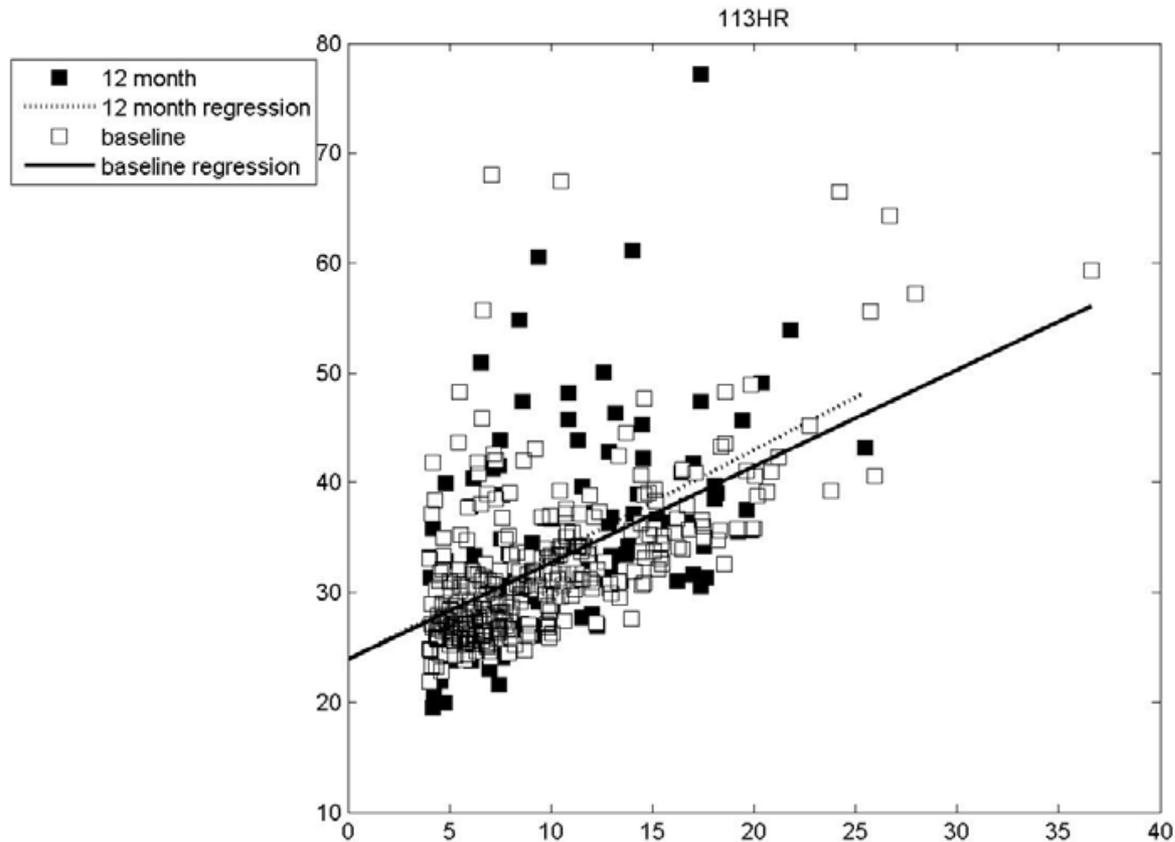
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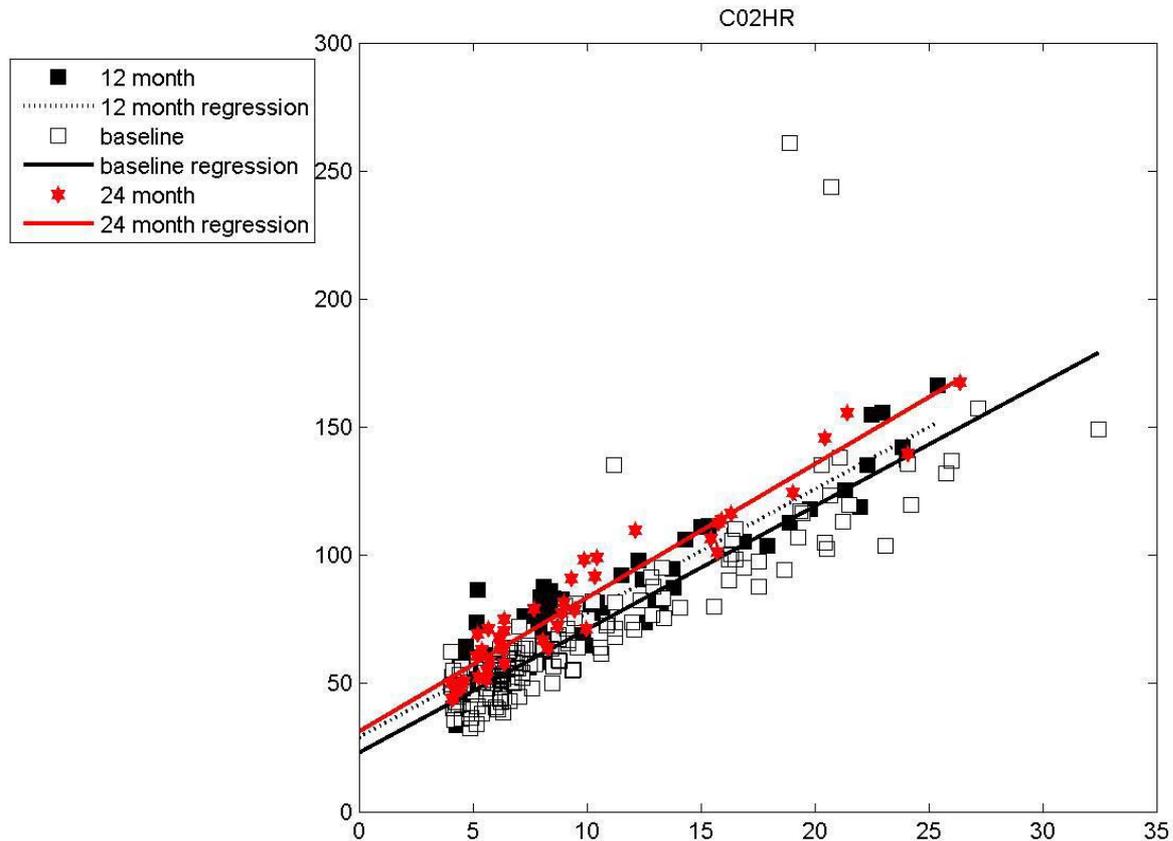
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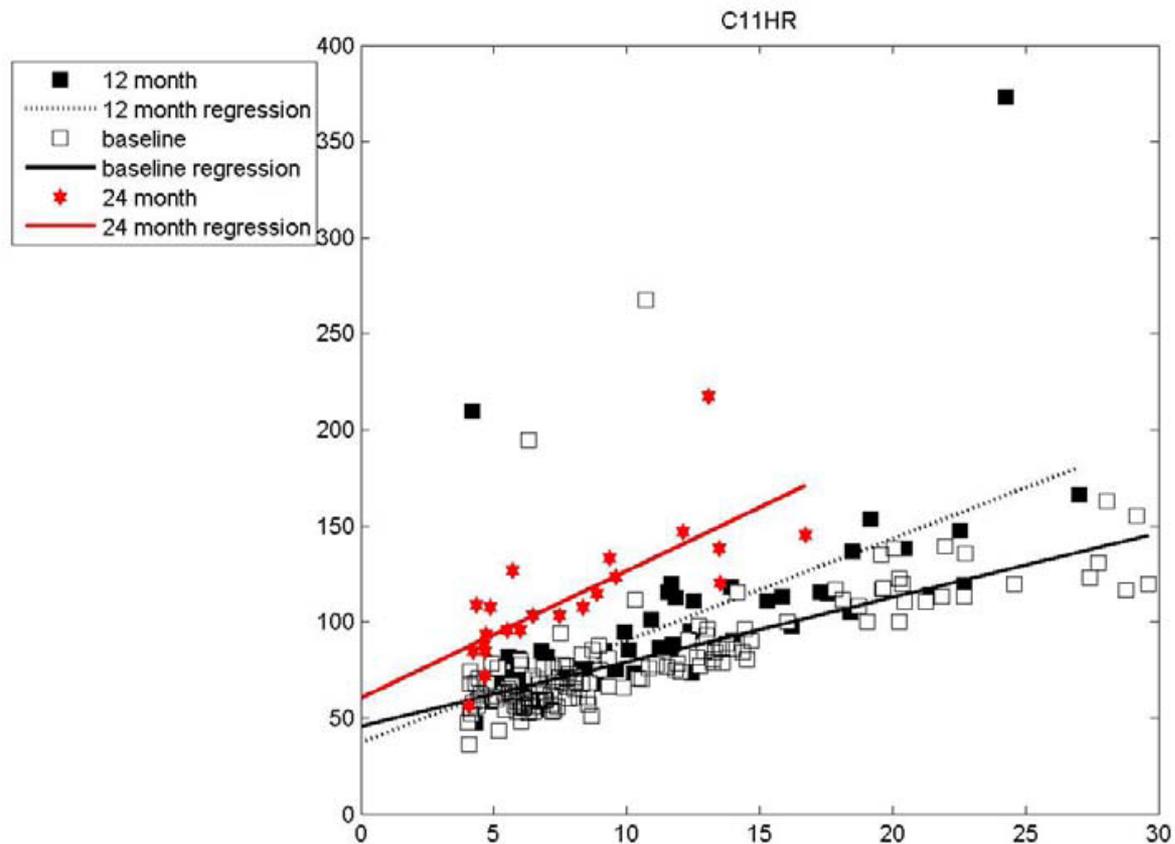
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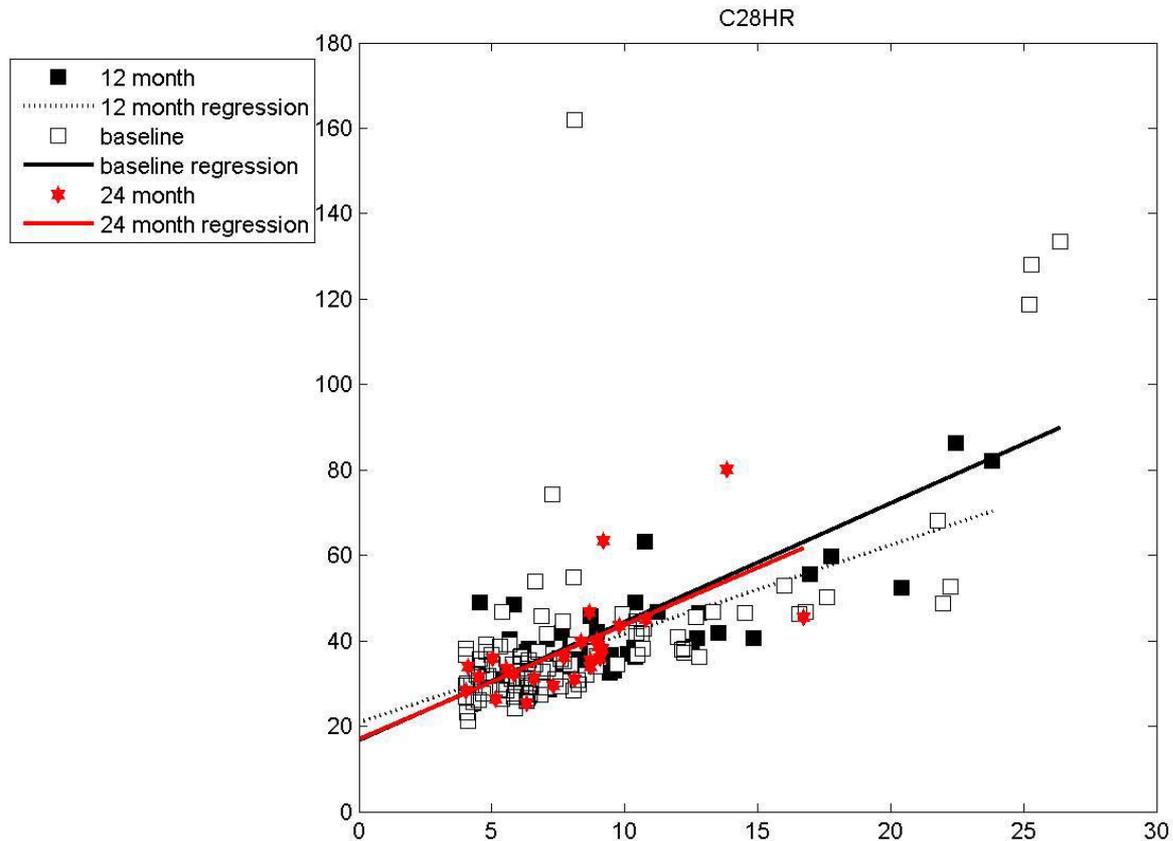
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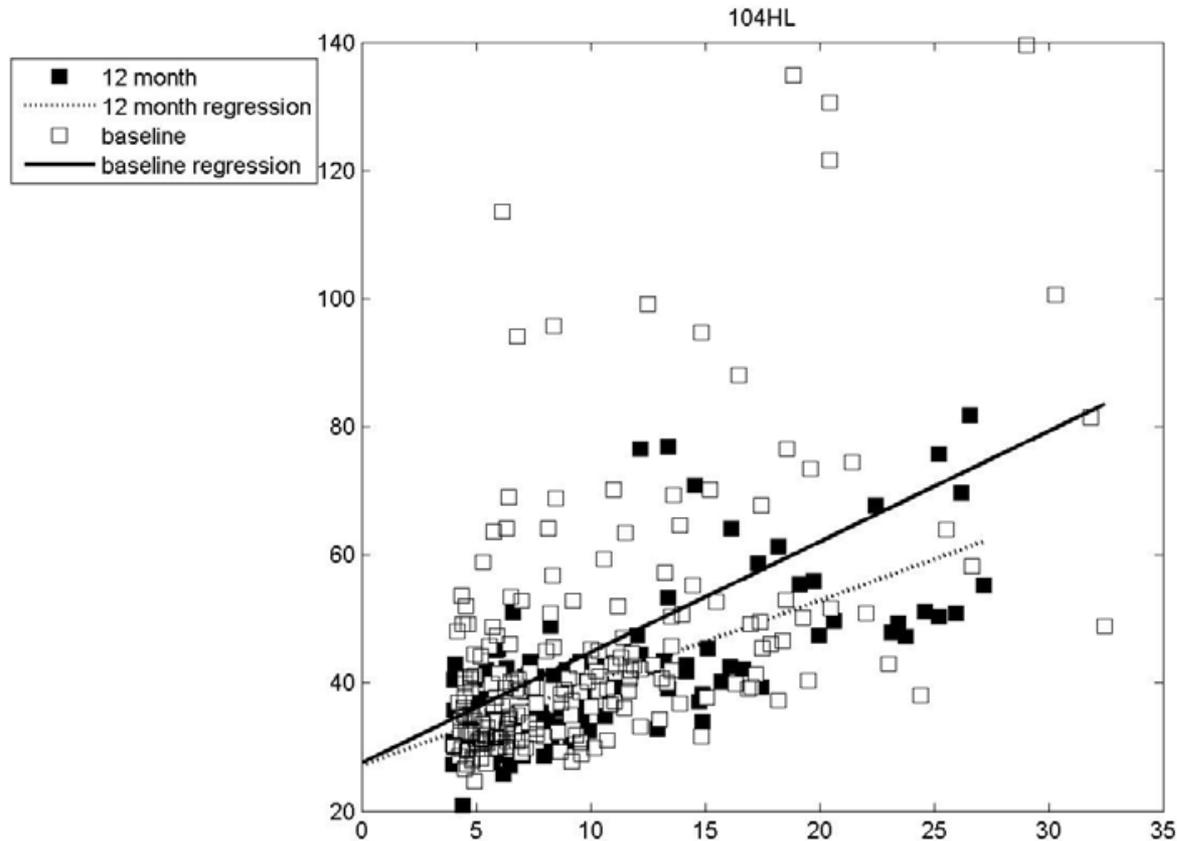
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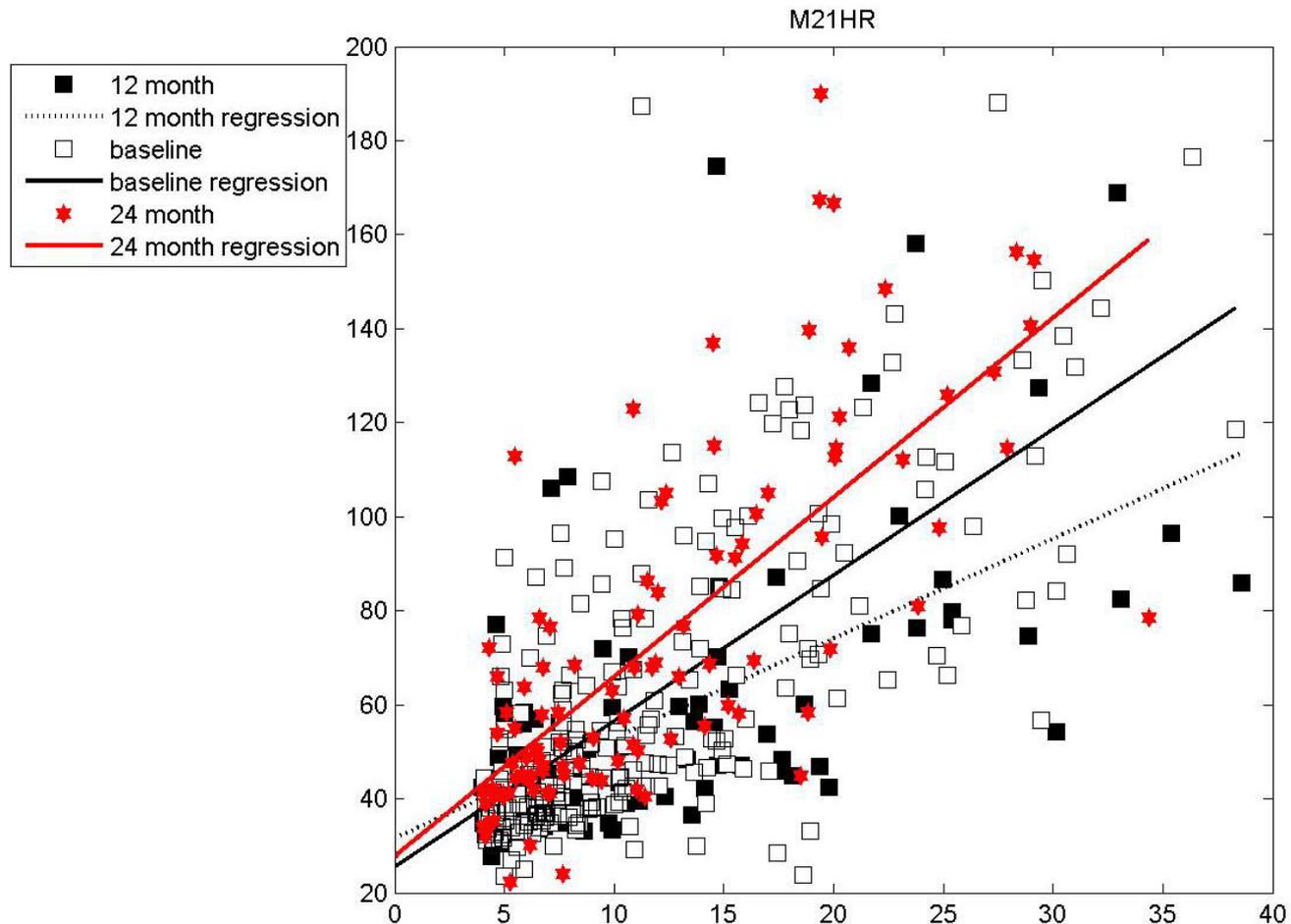
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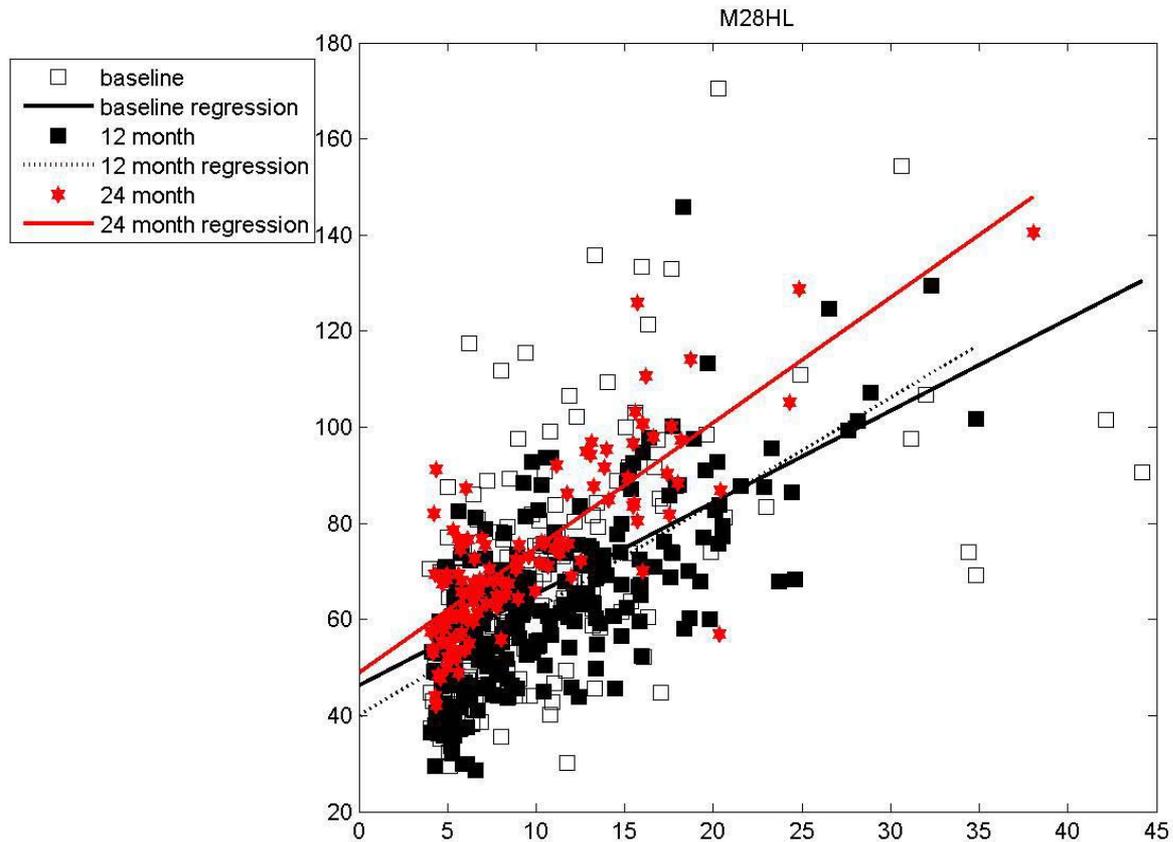
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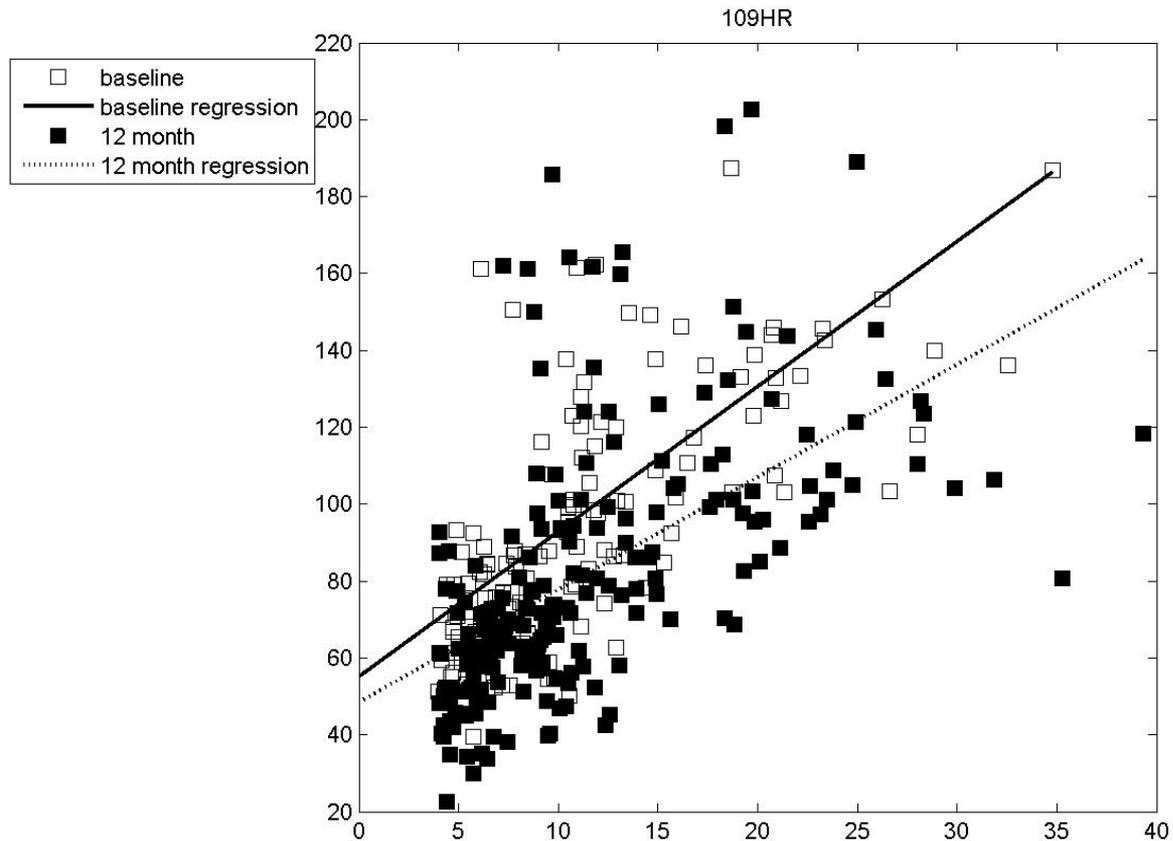
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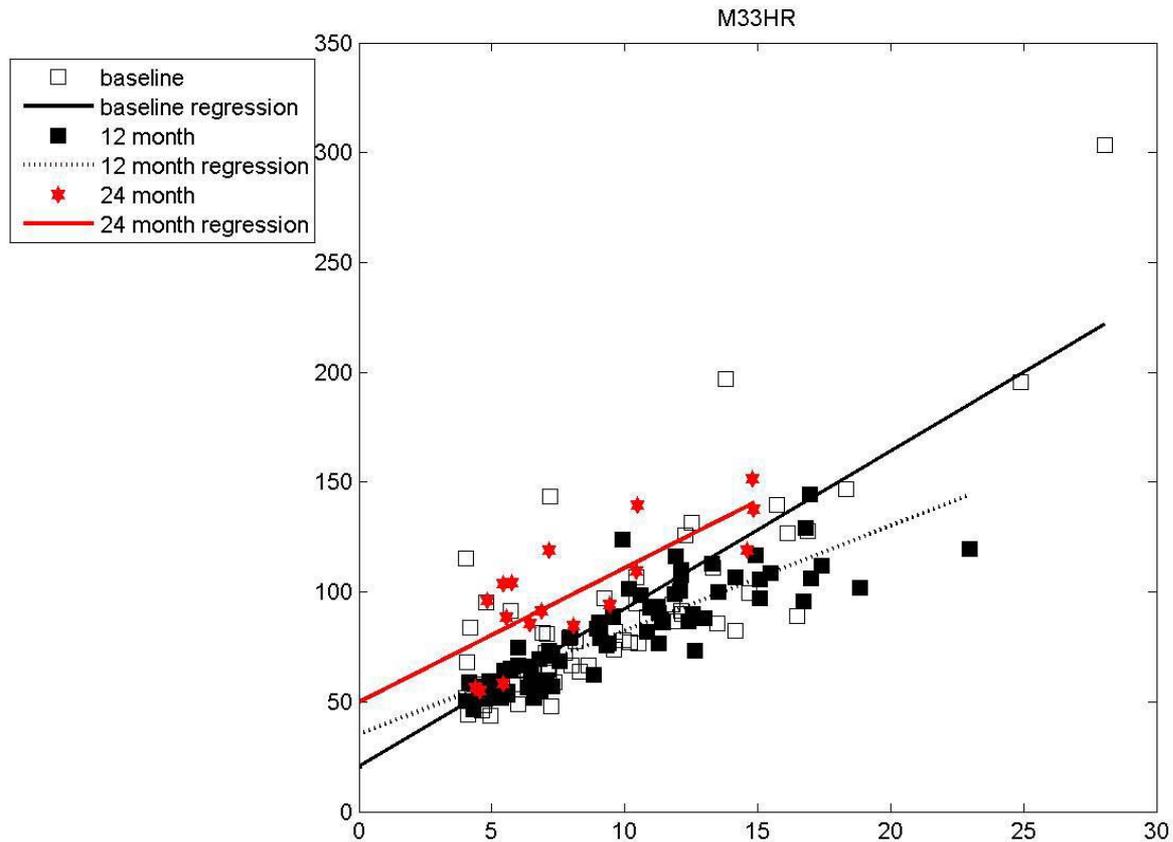
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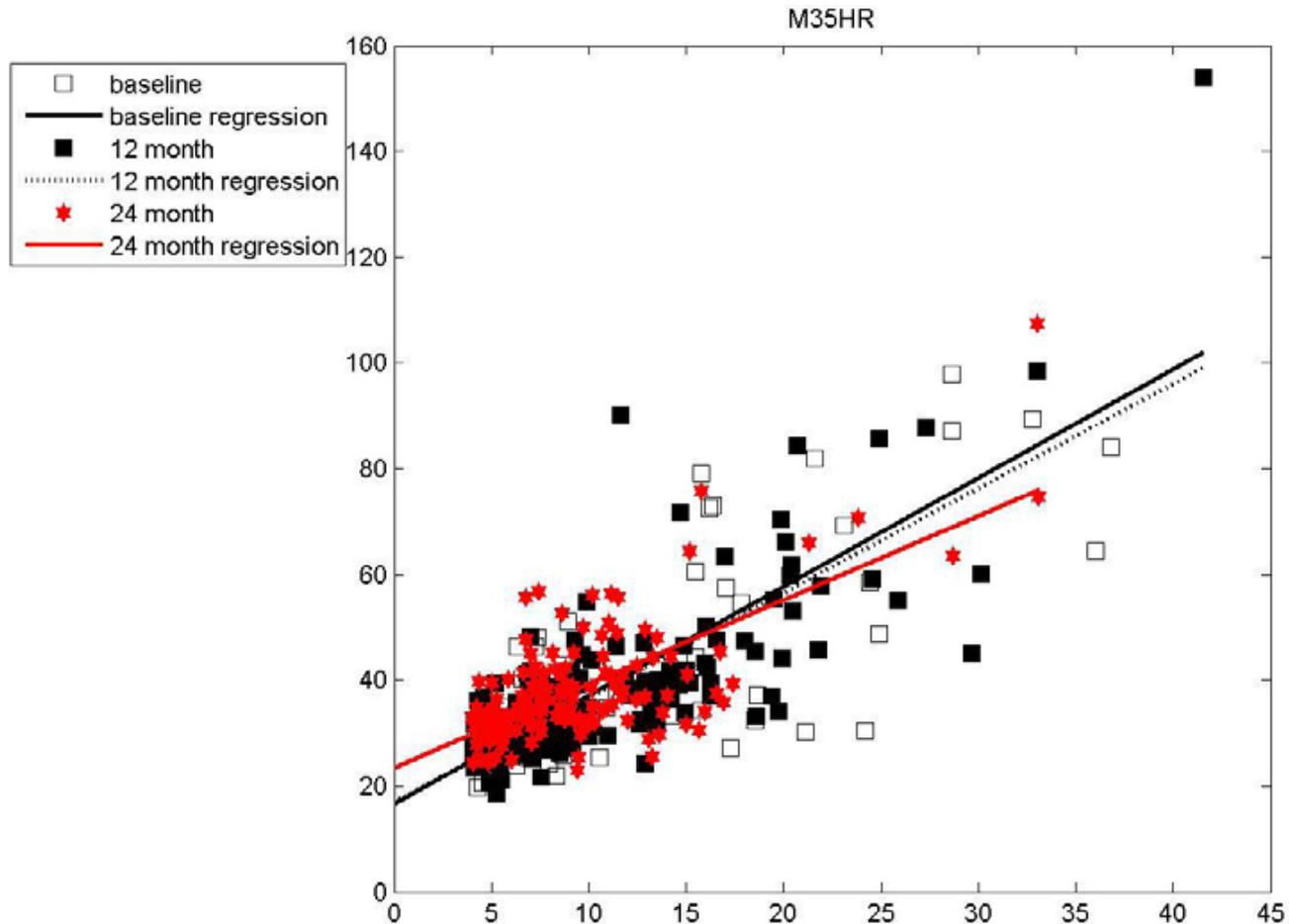
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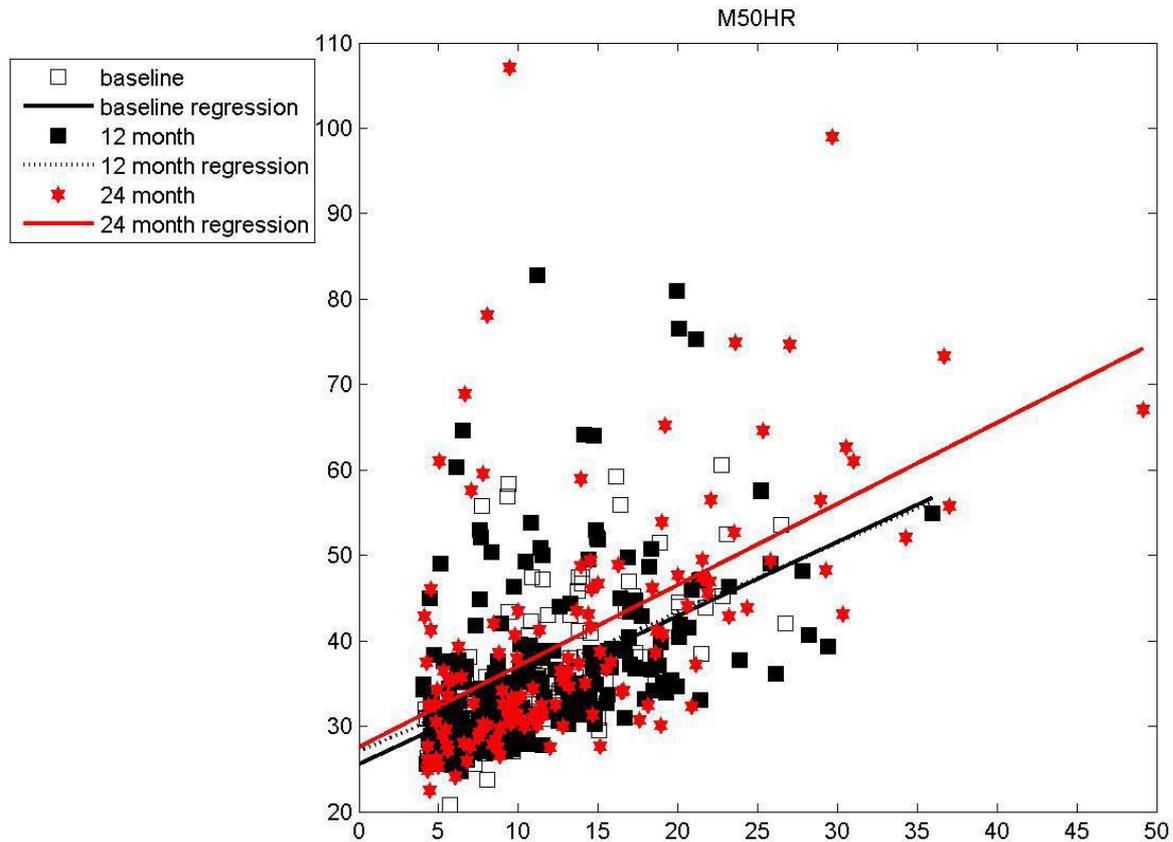
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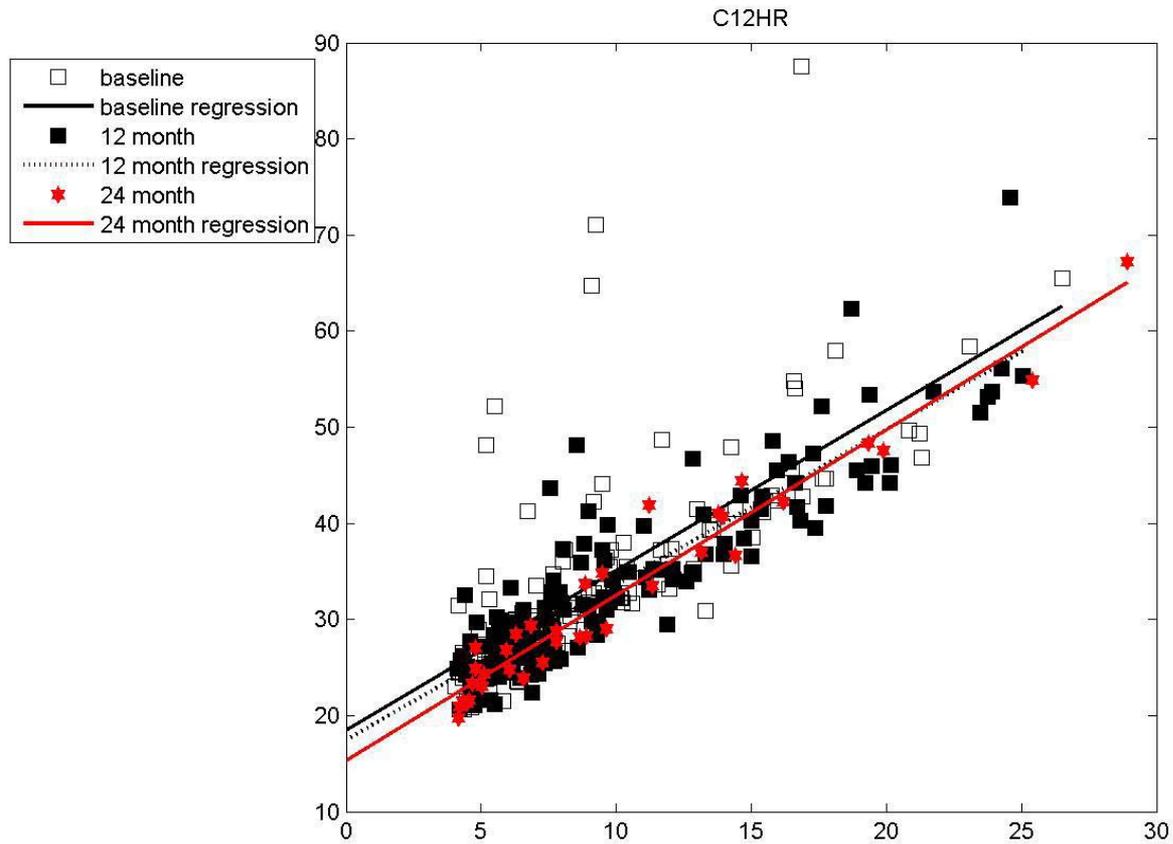
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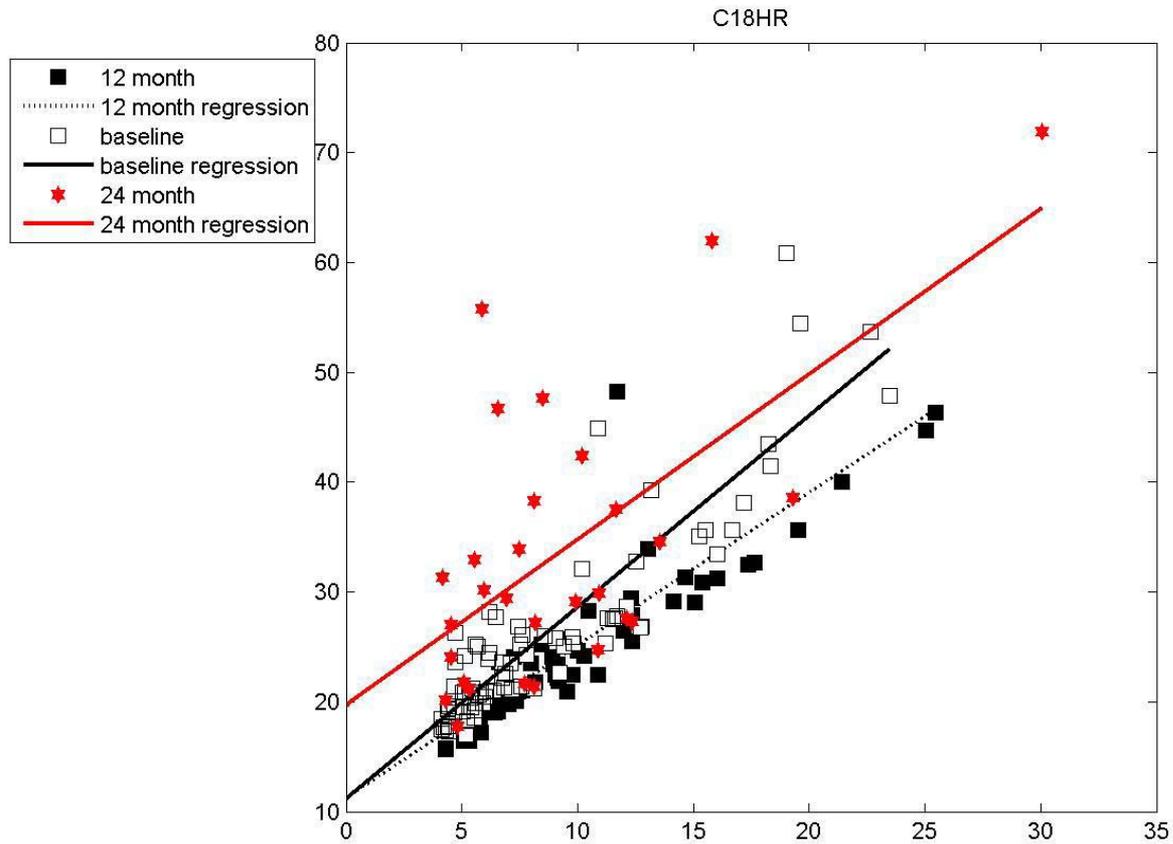
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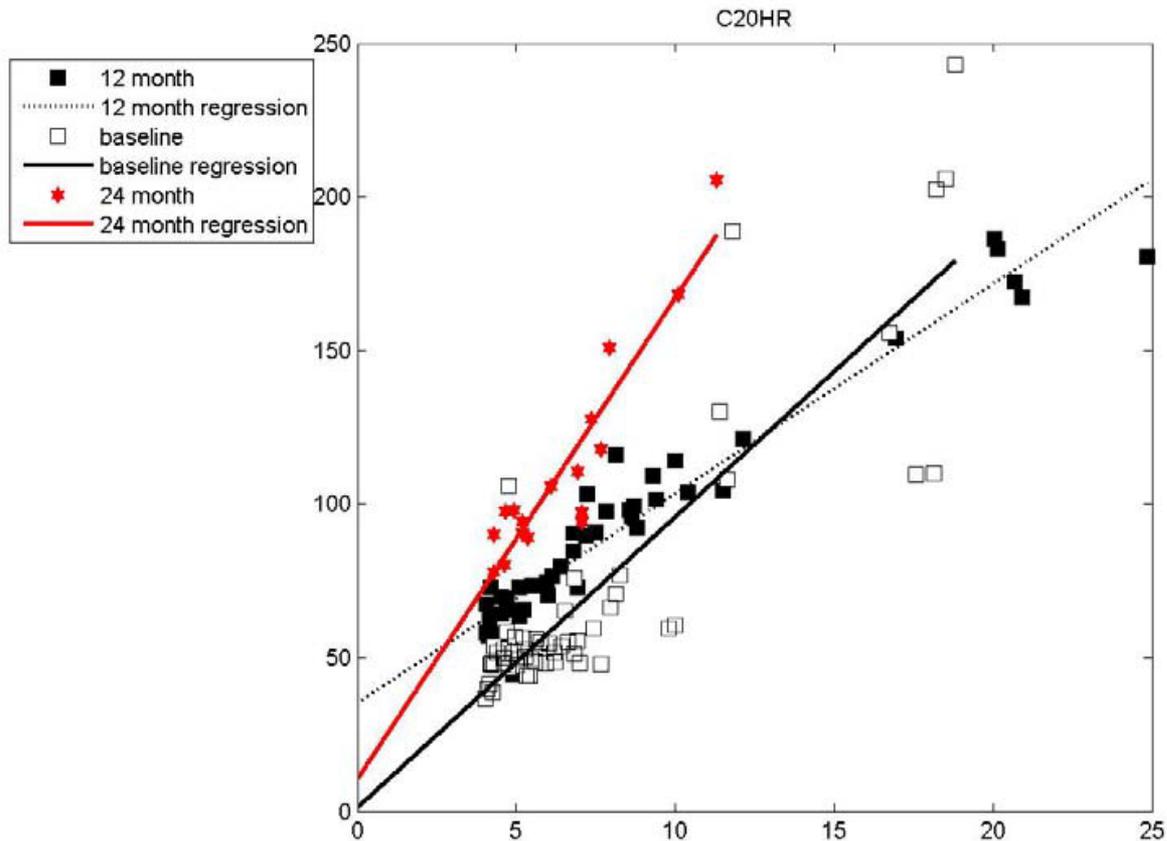
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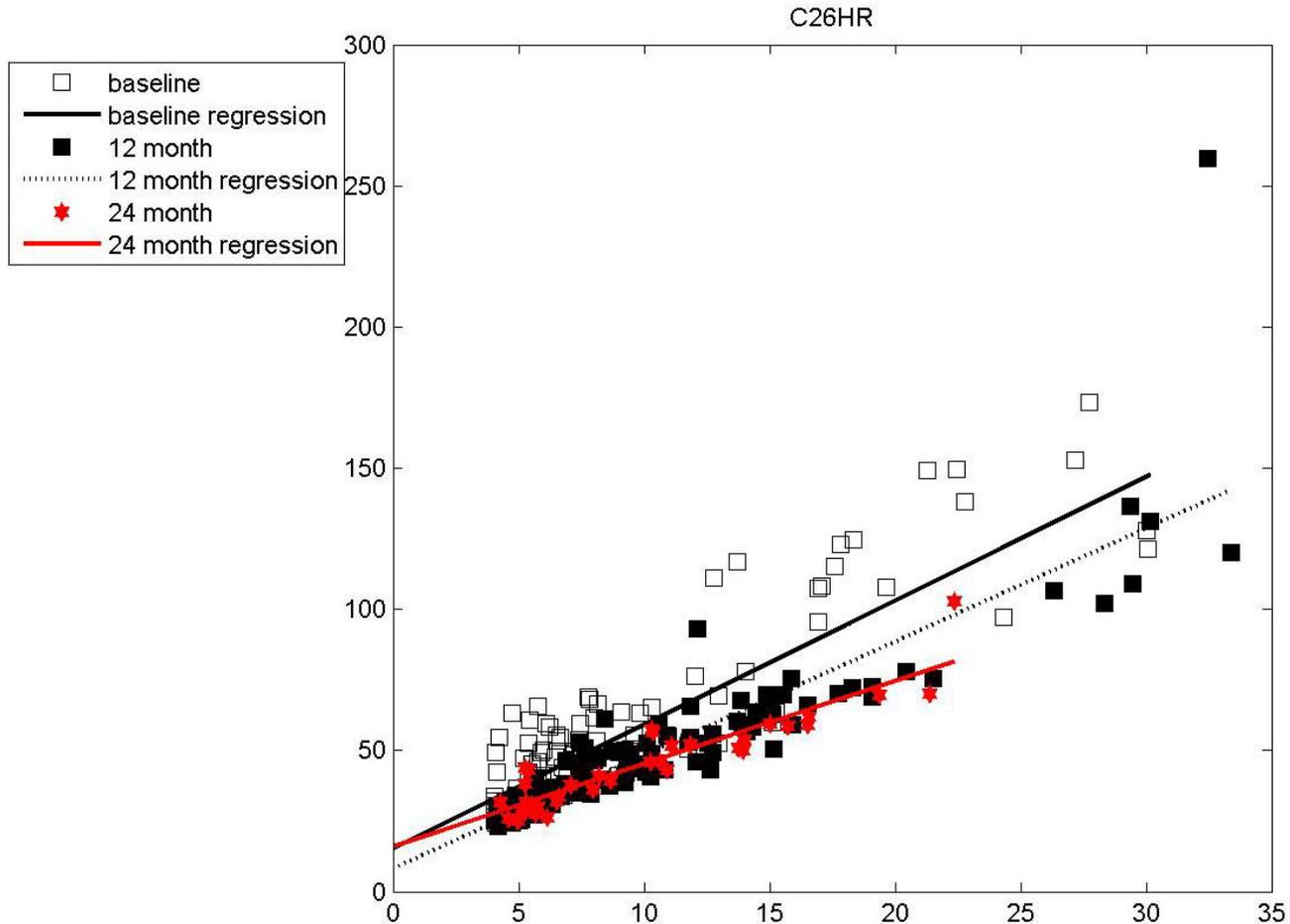
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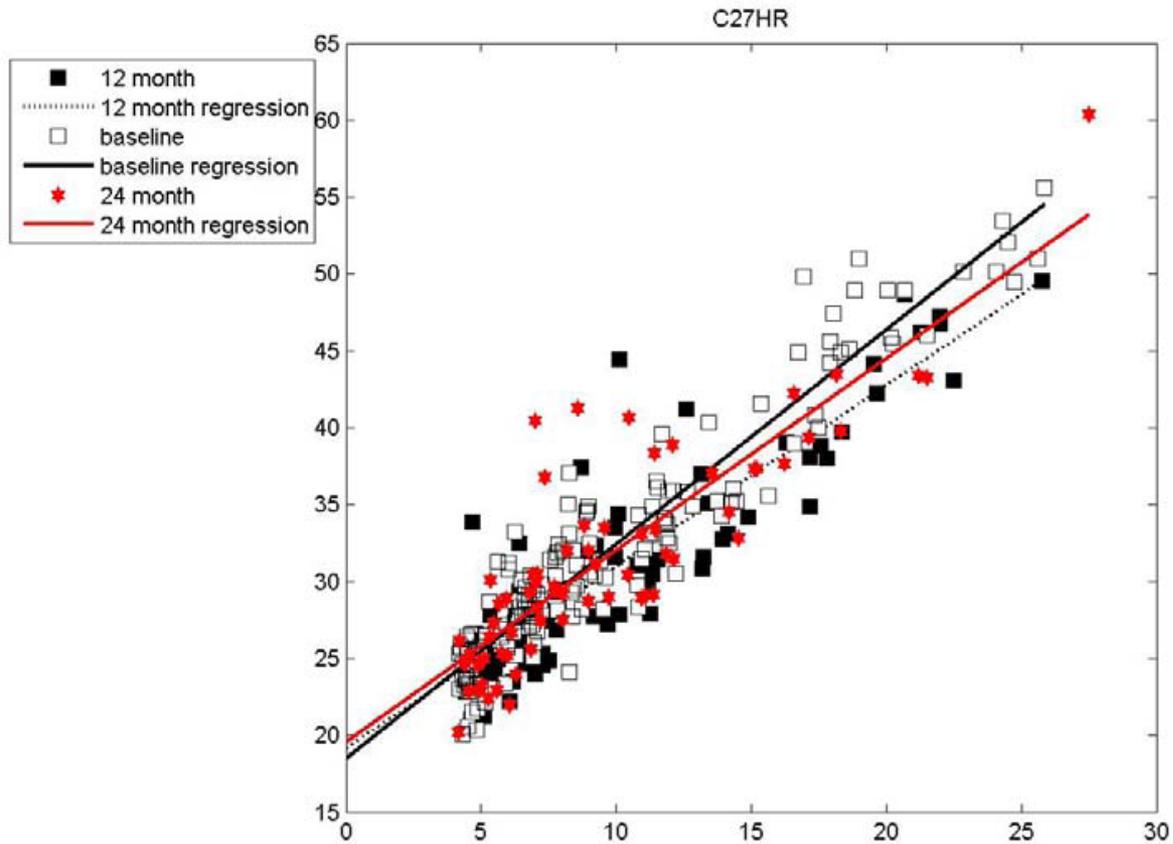
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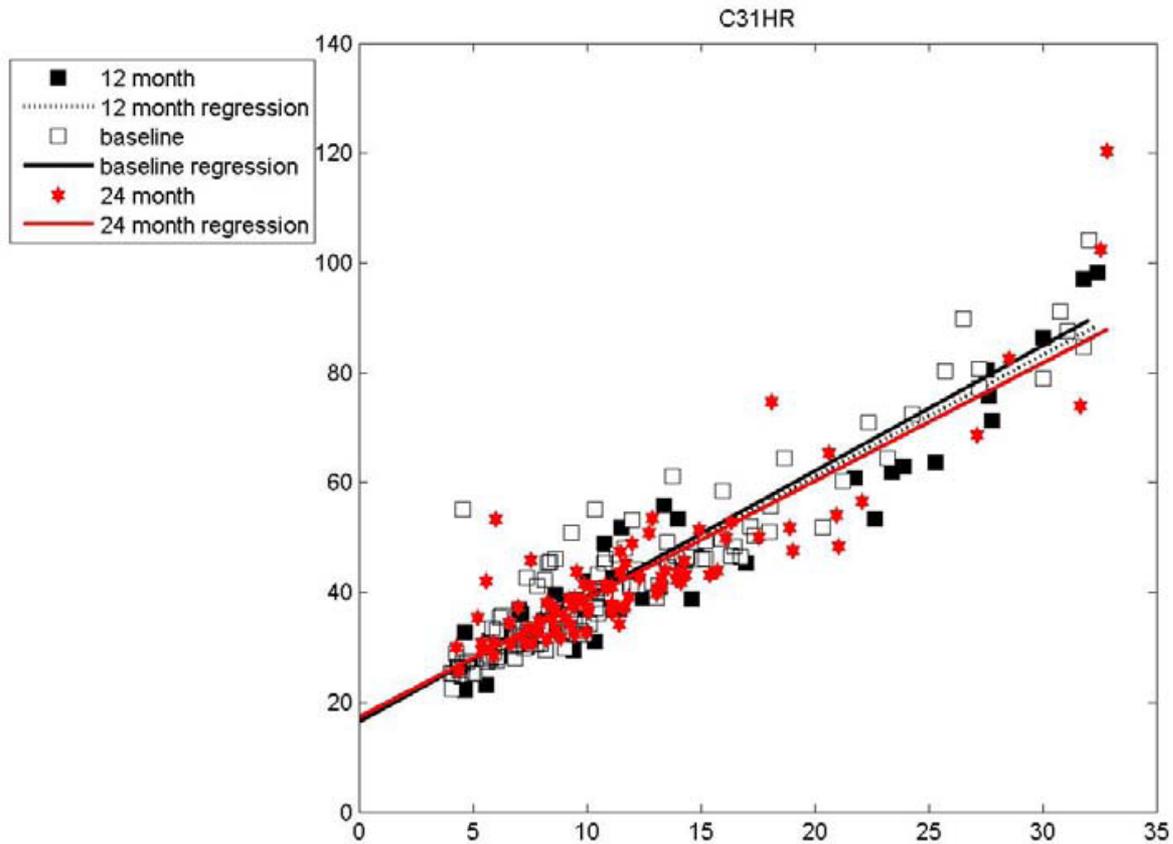
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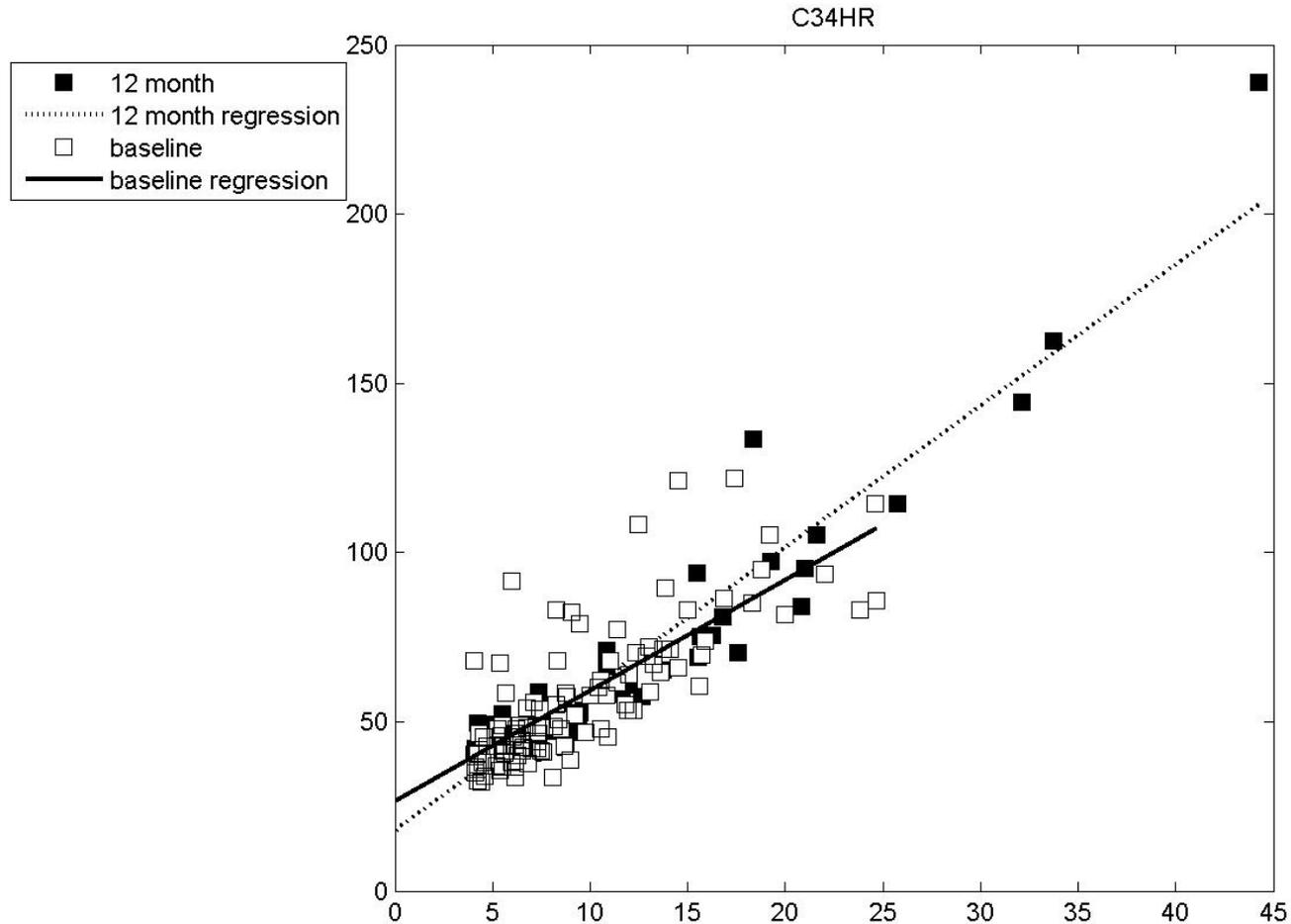
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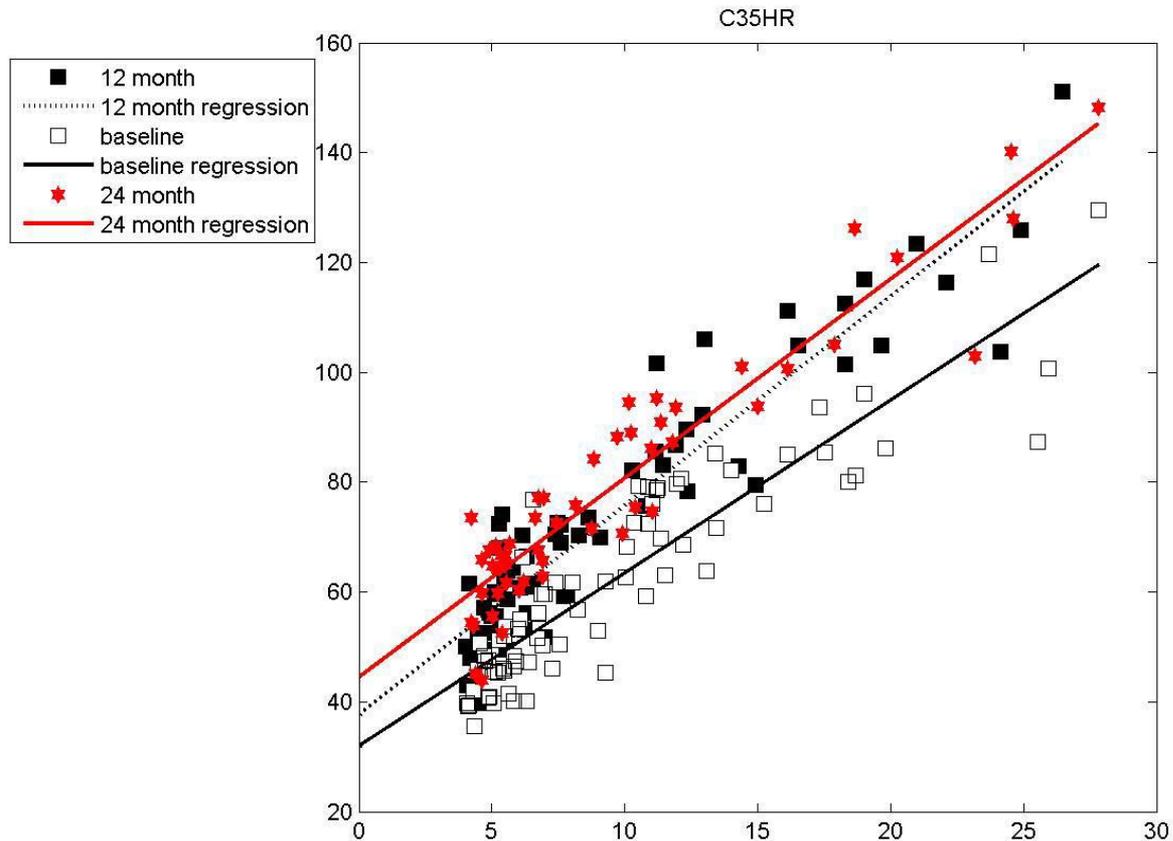
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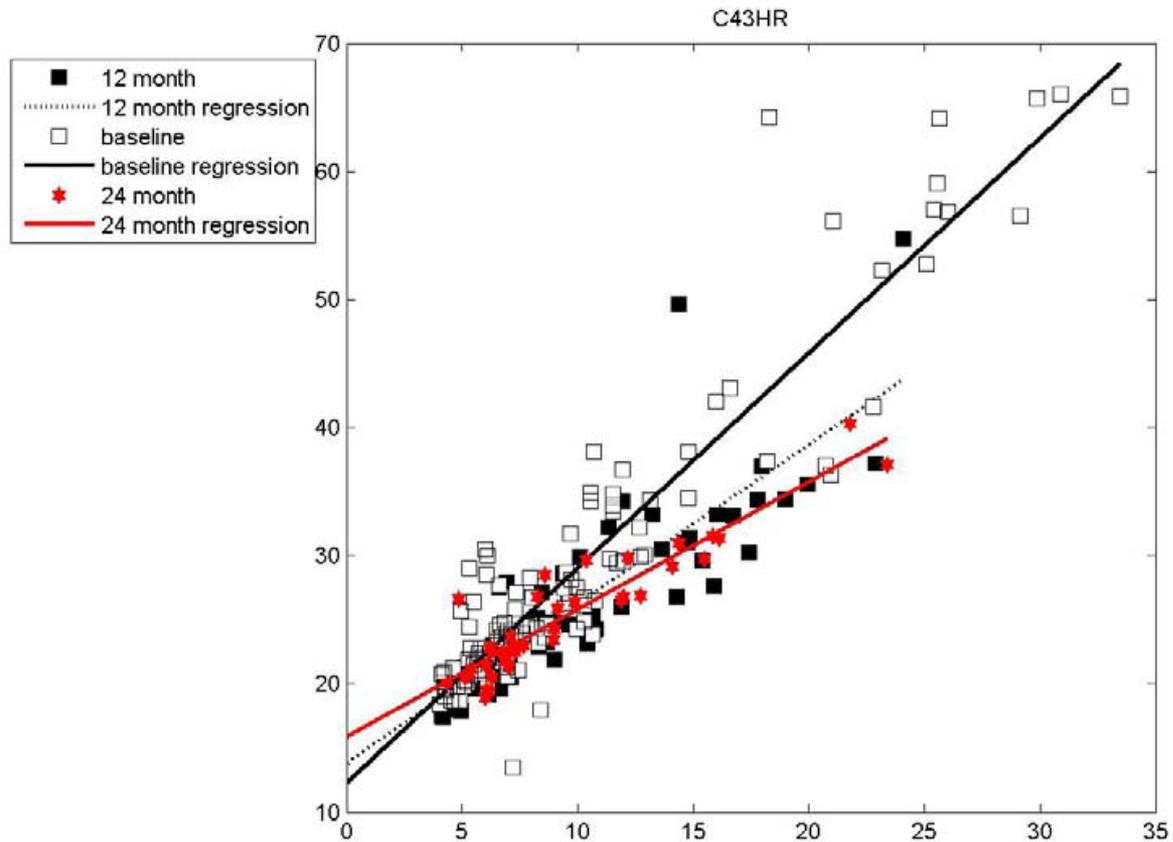
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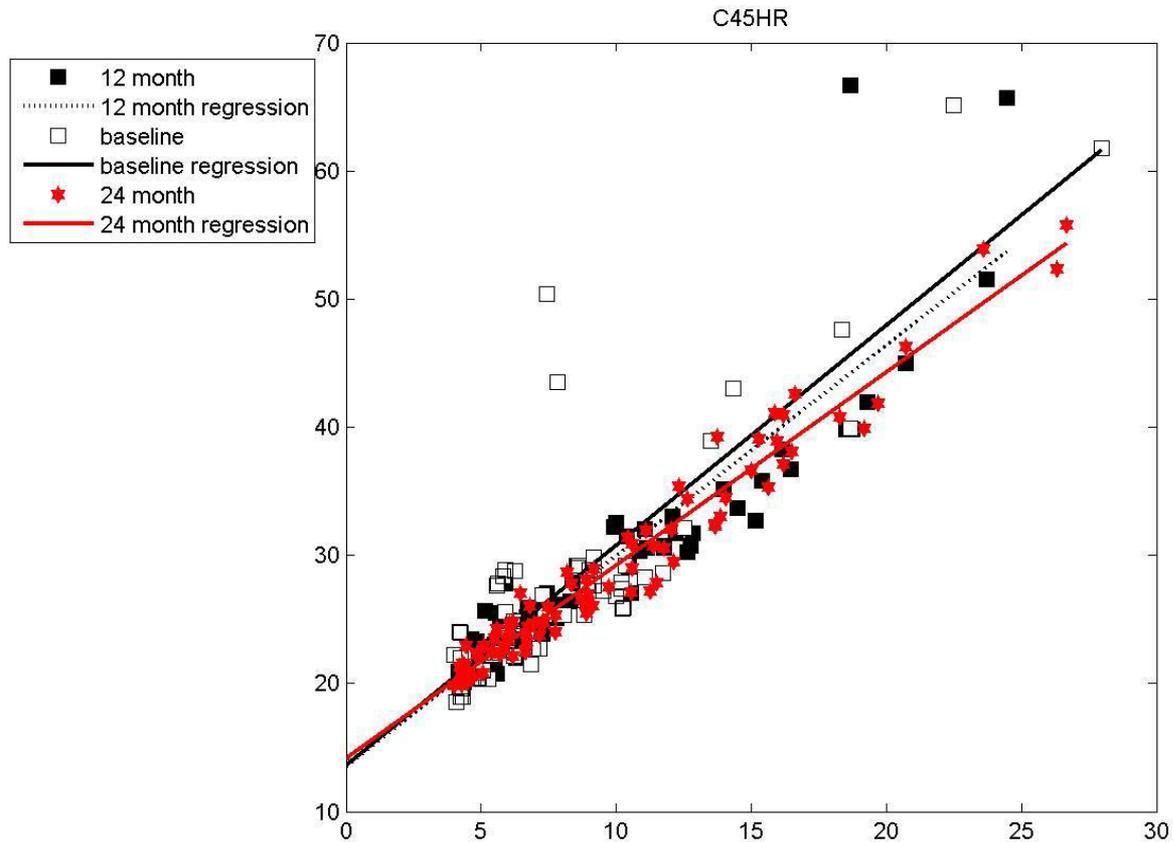
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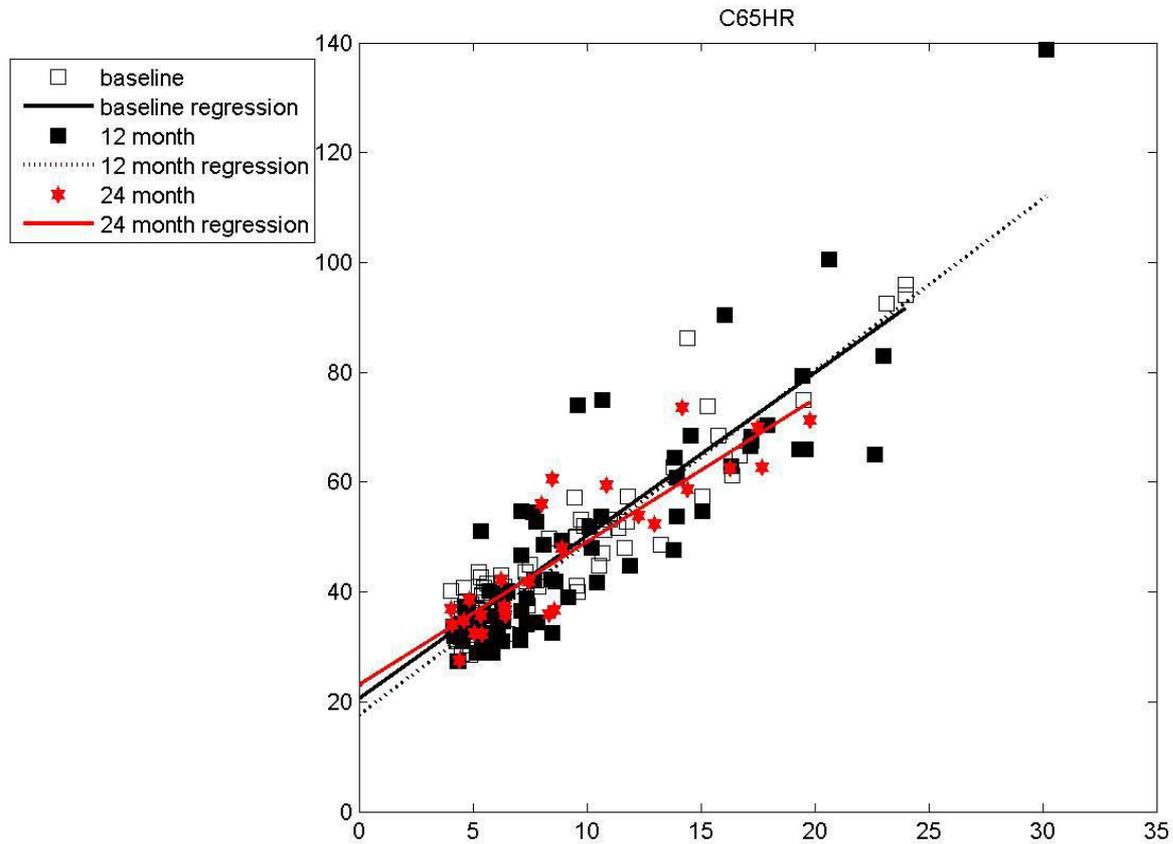
# 211 Treatment



# 214 Treatment



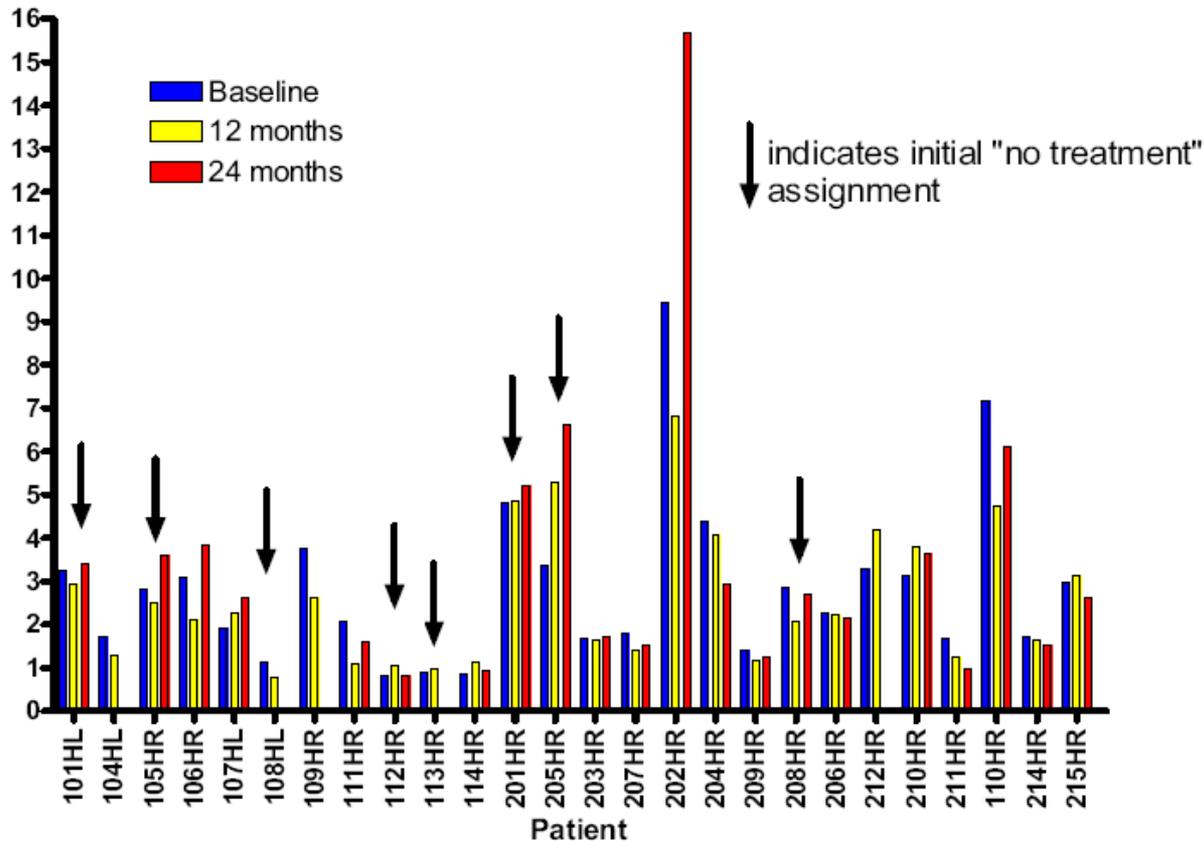
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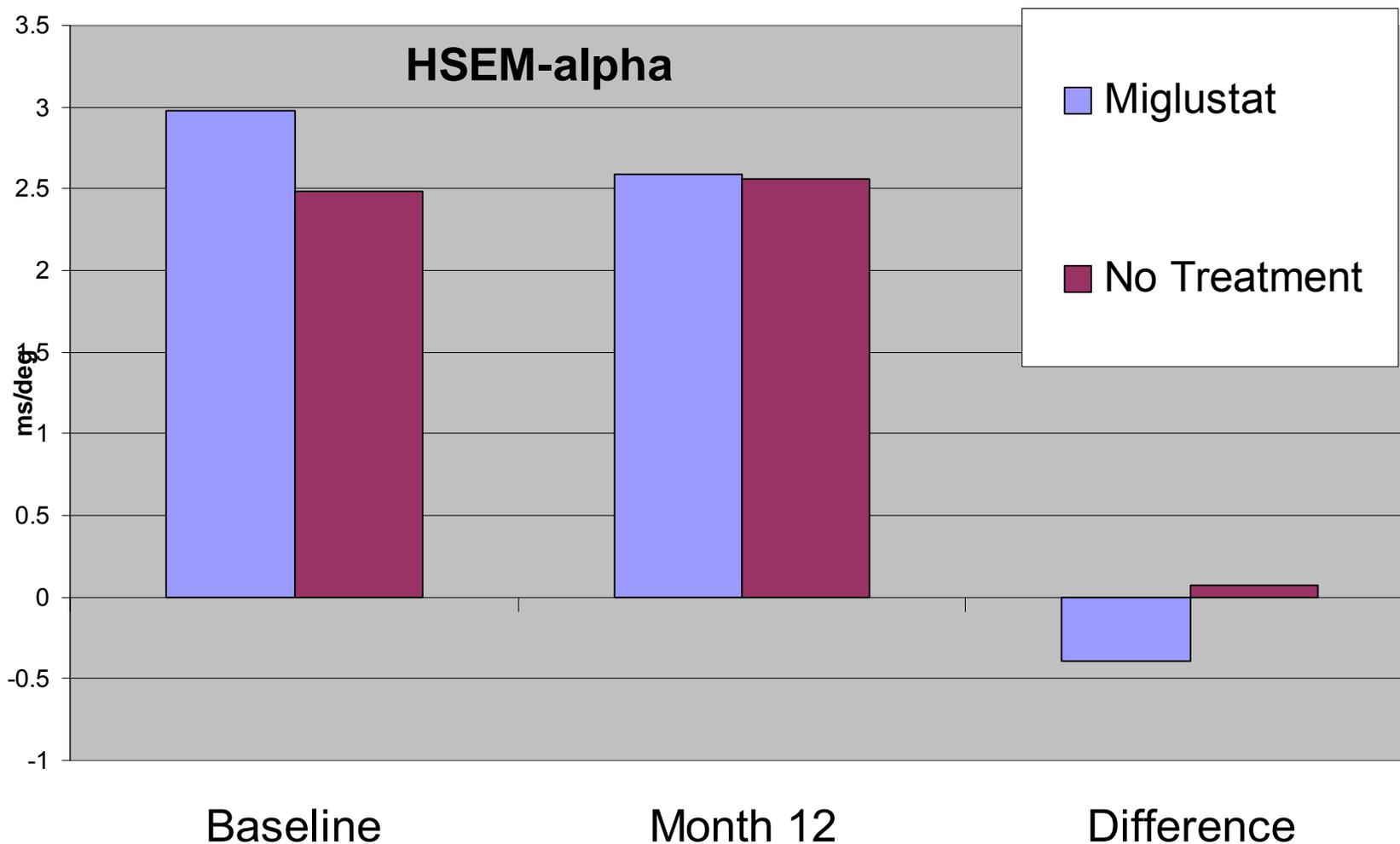
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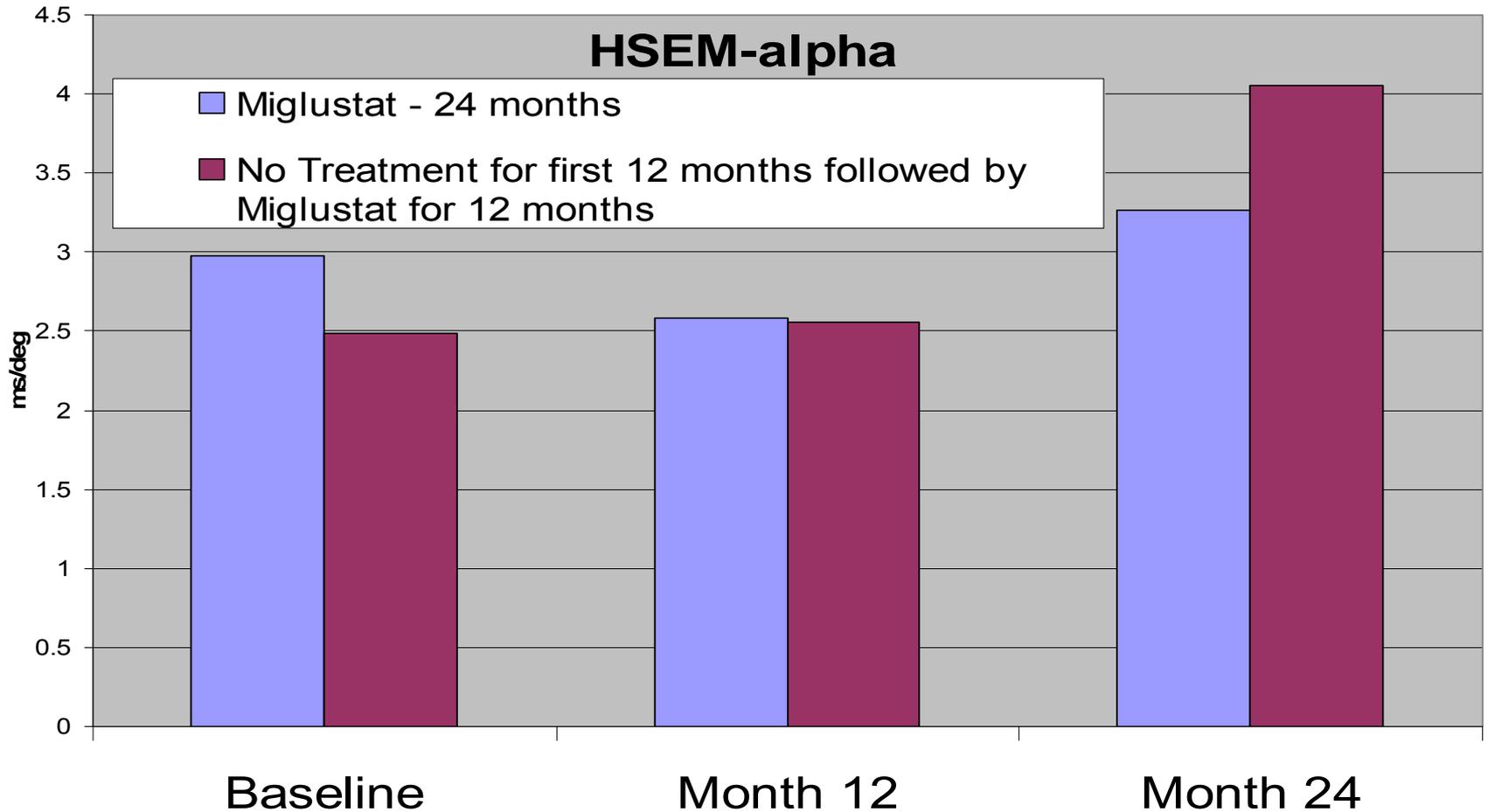
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**Differences are not statistically significant**

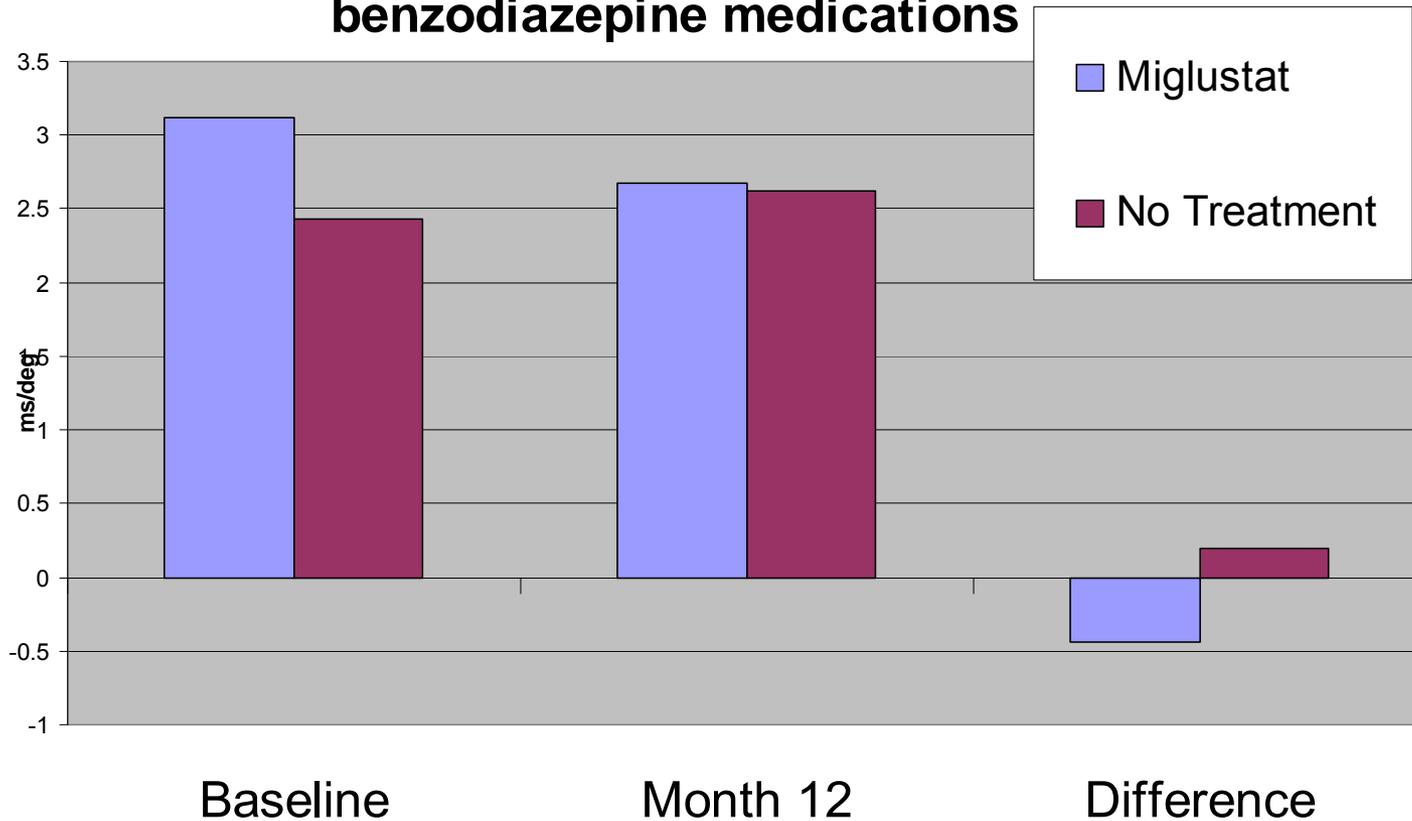


**Differences are not statistically significant**



## Removes “no treatment” patient with largest positive response

**HSEM-alpha excluding patients taking benzodiazepine medications**



# Conclusion

- Efficacy cannot be determined from saccadic eye measurements.