CAN EFFECTIVE BLEEDING CONTROL IMPROVE QOL FOR HAEMOPHILIA PATIENTS WITH INHIBITORS?

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STUDY OBJECTIVES

Document baseline Quality of Life (QOL) for haemophilia patients with inhibitors and examine changes during a trial (MAA-201) of subcutaneous marzeptacog alfa (activated), a novel FVIIa prophylactic agent

CONCLUSIONS

- The MAA-201 trial has demonstrated a significant reduction in proportion of days with bleeding using subcutaneous prophylaxis
  - Please attend the oral presentation OR11 on Friday 08 February 2019 08:30-10:00
- Subjects entering MAA-201 had worse QOL scores at baseline than reported scores for patients without inhibitors almost uniformly across domains
- After as few as 50 days of daily subcutaneous treatment with MarzAA, HAL and Haem-A-QOL scores were numerically improved compared with baseline

INTRODUCTION

- Haemophilia A or B morbidity increases throughout life
- Patients who develop neutralizing antibodies (inhibitors) (HPWI) to replacement clotting factor typically receive bypassing agents for episodic treatment of bleeds
- The short half-life of available agents for HPWI means prophylaxis is infrequently utilized, resulting in subjectively worse QOL, worse musculoskeletal outcomes and significantly higher mortality when compared with patients without inhibitors
- HPWI deserve improved prophylaxis
- QOL in hemophilia may be evaluated by Haem-A-QOL and impaired physical activity with Haemophilia Activity List (HAL)
- There is little data on QOL of HPWI compared with the broader population of hemophilia patients

METHODS

- We studied Marzeptacog alfa (activated) (MarzAA) an engineered rFVIIa with 4 amino acid substitutions and 9-fold greater potency than wild-type FVIIa given daily subcutaneously for prophylaxis in inhibitor subjects
- We evaluated the baseline scores of subjects in the MAA-201 trial using Haem-A-QoL[1] and HAL[2] and compared the results with those of subjects with severe haemophilia but without inhibitors recruited into a long-term prophylaxis trial[1] (A-LONG) and to published reference population baseline values for patients without inhibitors
- QOL scores were re-evaluated after 50 days of subcutaneous MarzAA and compared with those at baseline for 4 subjects who have completed the trial

BASELINE RESULTS

- Almost uniformly across domains, regardless of which QOL tool was used, subjects in MAA-201 had worse baseline scores than patients without inhibitors
- Mean baseline Haem-A-QOL summed score for A-LONG was 29.3 ±15.7 contrasting sharply with a much worse mean baseline summed score of 44.8 ±20.0 in the MAA-201 trial
- Using the more function-oriented HAL, MAA-201 median baseline scores were inferior across most domains compared with a reference population score

REFERENCES

[1] Su, J., Tsao, E., Feng, J., Myren, K.-J., & Glazebrook, D. (2017). Long-term quality-of-life outcomes with rFVIIIFc prophylaxis in adult subjects with severe hemophilia A. In ISTH, Berlin, Germany, (p. 416, Vol. PB 1783)

[2] Van Genderen FR, Westers P, Heijnen L. Measuring patients' perceptions on their functional abilities: validation of the Haemophilia Activities List (HAL). Haemophilia. 2006; 12(1): 36-46

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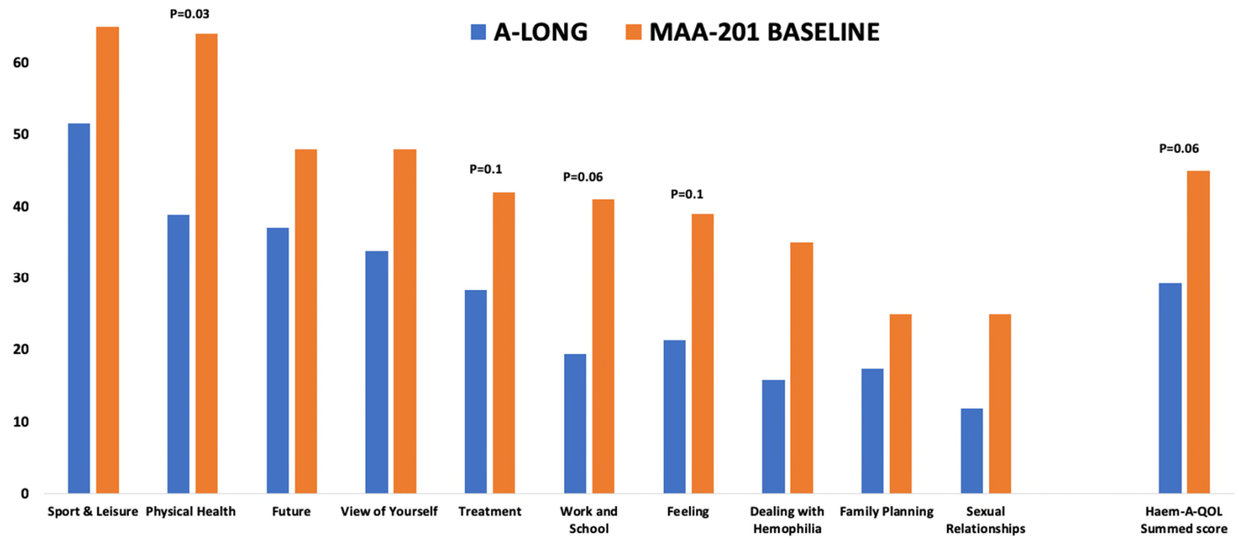
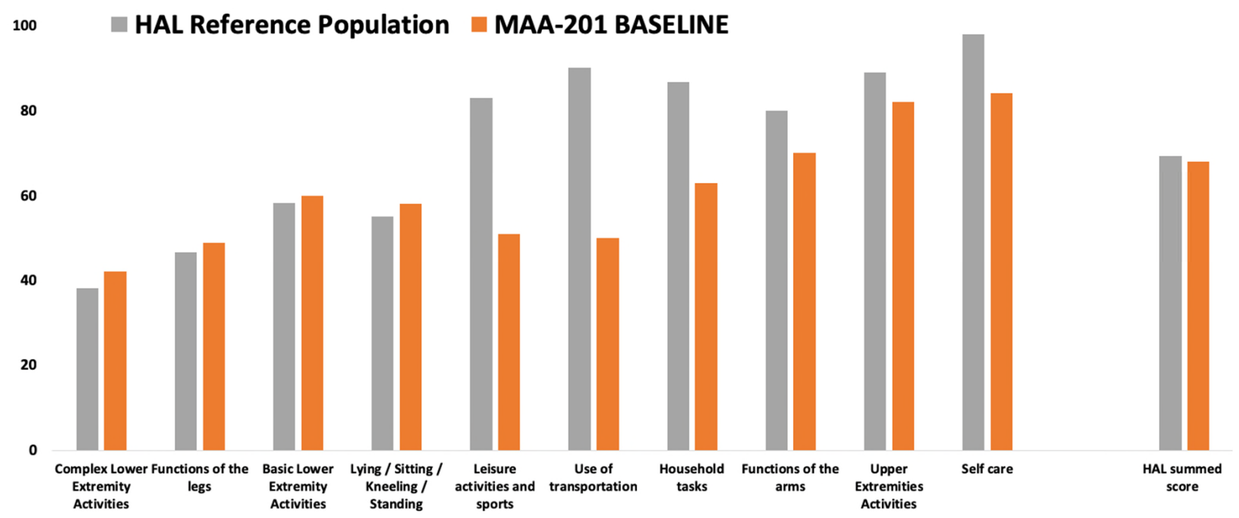
PATIENTS WITH INHIBITORS AT BASELINE IN MAA-201 HAVE WORSE MEAN HAEM-A-QOL SCORES COMPARED WITH PATIENTS WITHOUT INHIBITORS IN A-LONG[1]



In Haem-A-QOL, a score of zero represents normal function. Higher score represents *worse* disability

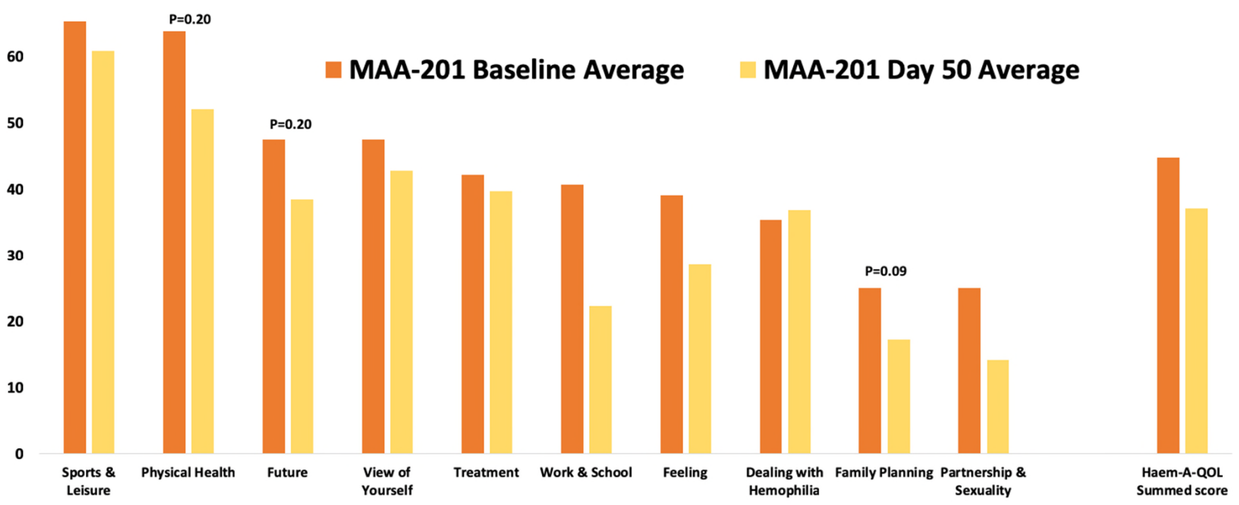
PATIENTS WITH INHIBITORS AT BASELINE IN MAA-201 HAVE WORSE MEDIAN HAEMOPHILIA ACTIVITIES LIST SCORES COMPARED WITH THE HAL REFERENCE POPULATION WITHOUT INHIBITORS[2]



In HAL, a score of 100 represents normal function. Lower scores represents *worse* disability.
Median values are reported for the reference population so statistical comparison is not possible.

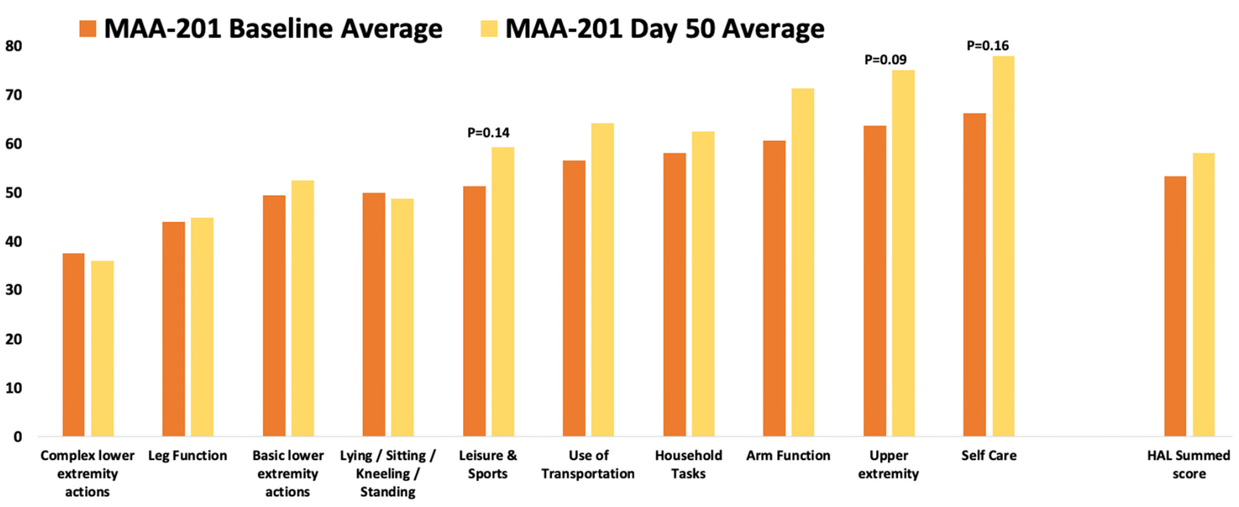
RESULTS FOR FOUR SUBJECTS AFTER TREATMENT IN MAA-201

AFTER 50 DAYS OF TREATMENT IN MAA-201 THE MEAN HAEM-A-QOL SCORES TRENDED TOWARDS IMPROVEMENT COMPARED WITH BASELINE SCORES



In Haem-A-QOL, a score of zero represents normal function. Higher score represents *worse* disability

AFTER 50 DAYS OF TREATMENT IN MAA-201 THE MEAN HAEMOPHILIA ACTIVITIES LIST DOMAIN SCORES TRENDED TOWARDS IMPROVEMENT COMPARED WITH BASELINE SCORES



In HAL, a score of 100 represents normal function. Lower scores represents *worse* disability

DISCLOSURES

H. Levy & F. Del Greco: Employees of: CATALYST BIOSCIENCES, F.V. McL. Booth paid consultant to CATALYST BIOSCIENCES. J Mahlangu Consultant and grant support from: CATALYST BIOSCIENCES