Comprehensive control of active systemic juvenile idiopathic arthritis and long-term outcomes with Canakinumab treatment

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OBJECTIVES

Multi-visceral involvement and complications of systemic juvenile idiopathic arthritis (SJIA) such as macrophage activation syndrome (MAS), may strongly decrease the life expectancy and quality of life (QoL) of SJIA patients. Canakinumab is the only IL-1 inhibitor approved for SJIA by the Food and Drug Administration and the European Medicines Agency. We aimed to estimate the long-term outcomes of canakinumab utilization in previously biologic-exposed SJIA Portuguese patients.

METHODS

We designed a discrete-time prediction model (figure 1) to estimate patterns of SJIA disease activity over time and predict life expectancy and quality-adjusted life years (QALY) in the long run. Extent of disease activity was assessed with the Juvenile Arthritis Disease Activity Score (JADAS) in 27 joints using the CRP level (JADAS27-CRP).

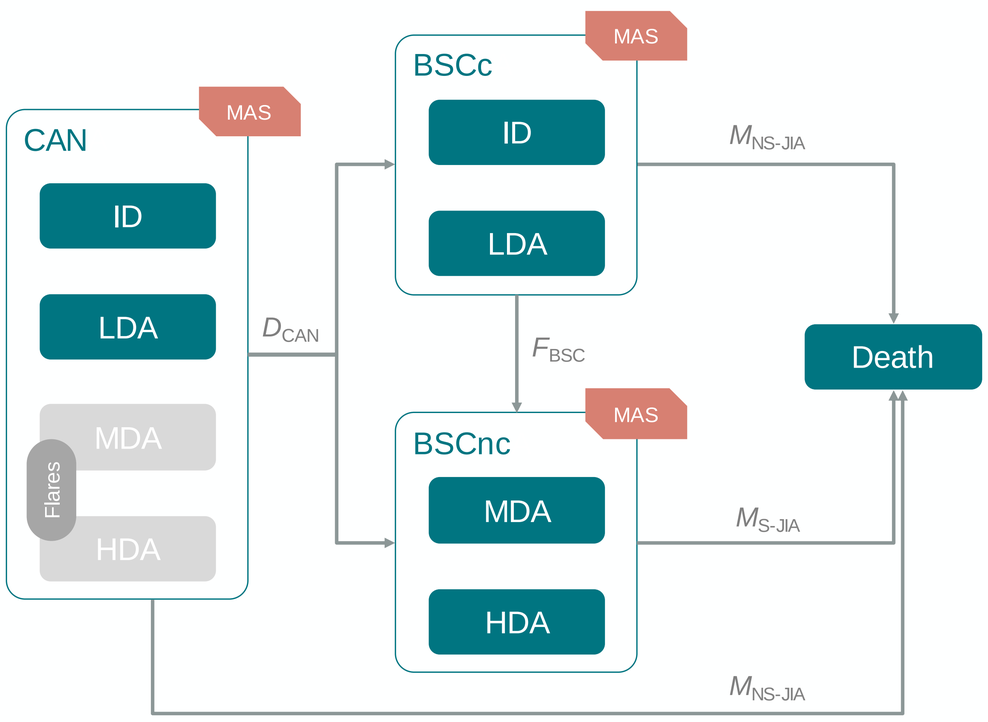

Figure1 Conceptual model for treatment and outcomes in systemic juvenile idiopathic arthritis

Legend – HAD (high), MDA (moderate), LDA (low), disease activity; ID - inactive disease; CAN - canakinumab; D_{CAN} – discontinuation CAN; BSC best supportive care; F_{BSC} – flares increased in disease activity with BSC; M - mortality, MNS-JIA non systemic juvenile idiopathic arthritis related mortality.

Data on the efficacy and QoL (EQ-5D-3L) for canakinumab is from the clinical trials ß-SPECIFIC 2 (NCT00886769), ß-SPECIFIC 3 (NCT00891046), and ß-SPECIFIC 4 (NCT02296424). Time to event analysis was used to assess the occurrence of persistence on treatment with canakinumab (***D***$_{CAN}$), disease remission with inactive (ID) or low disease activity (LDA), disease flares, MAS and SJIA related (***M***$_{S\_JIA}$) and non-related mortality (***M***$_{NS\_JIA}$). Country specific QoL preferences supported QALY estimation. Markov Chain Monte Carlo methods were used to simulate posterior distributions of the outcomes of interest.

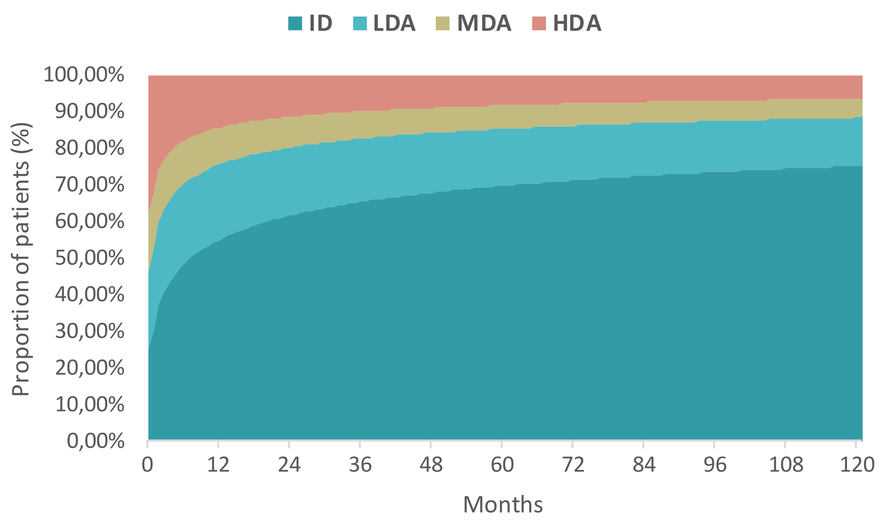

Figure 2 Evolution of disease activity (JADAS27-CRP) in SJIA patients treated with canakinumab

RESULTS

We simulated through lifetime a cohort of systemic juvenile idiopathic arthritis patients with mean age of 9 years old and composed of 39% of males, with HDA high (91.7%) or MDA moderate (8.3) disease activity at treatment initiation. Time in remission (ID in figure 3) is maximized with canakinumab treatment to 17.7 years (95%CI: 10.6-25.6). A significant reduction of 15.6 years (95%CI: 9.8-17.7) spent in high SJIA activity is expected with canakinumab treatment, leading to an incremental 7.2 QALY gain (IC95%: 4.5-8.3) (Figure 3).

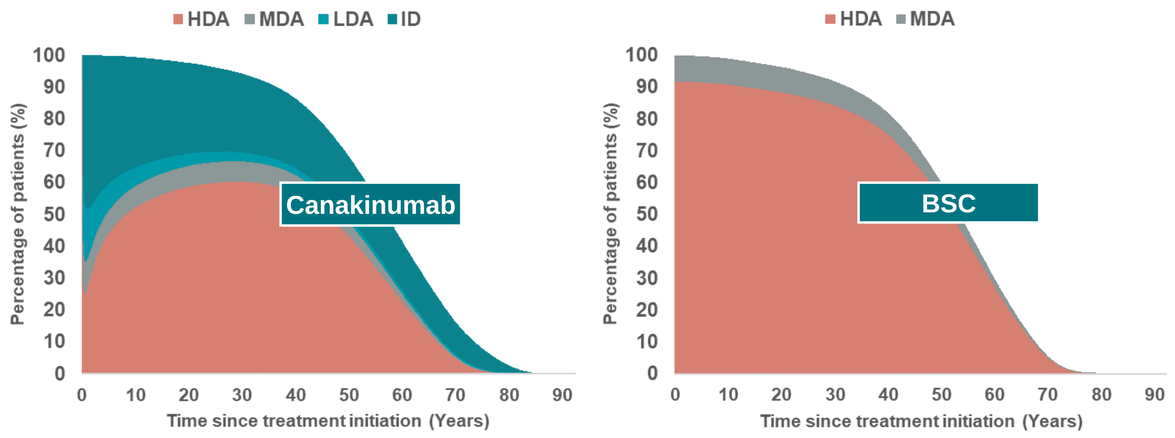

Figure 3 Lifetime effectiveness of canakinumab treatment and BSC in previously biologic-exposed SJIA patients

Life expectancy is expected to increment by 4.1 years (95%CI: 2.0-6.5) with canakinumab treatment relative to the natural history of disease (Figure 4). Better disease control and longer life expectancy is estimated to result in substantial QoL gains of 10.8 QALYs (95%CI: 6.3-15.5). Sequential canakinumab tapering from 4 mg/kg to 2 mg/kg every 4 weeks with further reduction from 2 mg/kg to 1mg/kg of canakinumab every 4 weeks, and ultimately interruption of canakinumab due to disease control, allows health resource optimization while maintaining disease control for an extra 5 months (95%CI; 3-7).

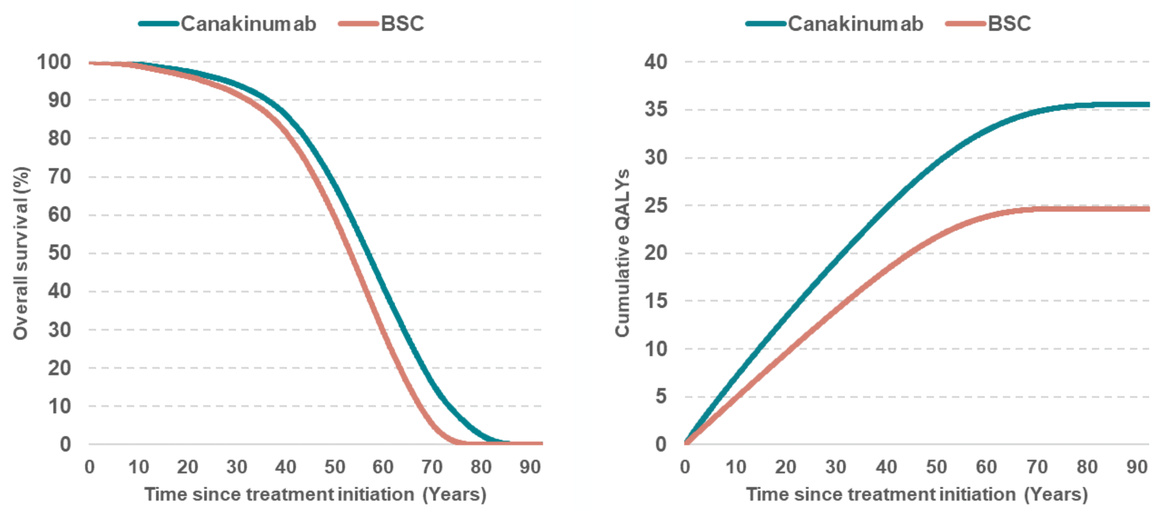

Figure 4 Estimated overall survival and quality adjusted life years (QALYs) of canakinumab treatment relative to BSC in previously biologic-exposed SJIA patients

= CONCLUSIONS

Comprehensive control of disease with canakinumab maximizes long-term outcomes for previously biologic-exposed SJIA patients and may impact the natural history of systemic juvenile idiopathic arthritis.

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