AL amyloidosis survival evolution in new agents era : A real life experience

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Introduction

Light chain amyloidosis (AL) is a rare but severe disease due to deposition of misfolded protein in tissues leading to progressive organ failure. Its prognosis is mostly due to the degree of cardiac involvement at diagnosis.
In the past years, thanks to the introduction of new agents, such as Daratumumab, a huge improvement of the prognosis has been observed due to better efficacy and less toxicity as well.

Objectives

This retrospective review aimed to evaluate the reported improvement in a real life population. For this purpose, we looked at our entire AL patients population during the past 15 years.

Method

We collected the data of 42 AL patients from two hospitals in Brussels from 2006 until 2019 and separated them into two periods, before and after the use of Daratumumab in Belgium (2015). We looked into and then compared overall survival (OS), progression free survival (PFS), toxicities but also severity of organ involvement at diagnosis and time from first symptoms to diagnosis between 2006-2015 and 2015-2019.

Results

Basics characteristics of the two groups were comparable with no significant difference observed.
At diagnosis, there was no difference between the two cohorts regarding the number of organ involvement and their severity (stage 4 Mayo Clinic 23 vs 25% respectively, p=1). In particular, the amount of cardiac involvement was comparable (77 vs 70% respectively, p=0.72).
We haven't observed any improvement concerning the time nto establish the diagnosis from first symptoms described by patients (109,5 months versus 181 months, p=0.3) between the two periods of time.
The median OS (mOS) during the 2006-2015 period was 7 months while it was not reached during the second one (p=0.01). However, the median PFS (mPFS) was not different (7 months) as was the quality of the response to treatment (≥ VGPR in 41 vs 42.5 % respectively, p=0.74).
Within the specific population of patients treated by Daratumumab (N=12), we described a significant improvement of mOS and mPFS compared to other treatments.
Toxicities were much less in that specific group of patient, with only some infectious (25%) and haematological (17%) complications of > grade 2.

Conclusions

We observed a significant improvement in overall survival as described in other recent and larger publications. These encouraging results are mostly due to the introduction of new

agents, especially Daratumumab which confers fast and durable response leading to organ improvement later on. Also, new guidelines recommending to switch treatment quickly if no satisfactory response is reached, are part of this success.
However, even if a massive effort has been done in the recent past years by scientific authorities to improve the time to diagnosis (recommendation of MGUS screening i.e.), we observed no difference concerning the number of severe cases at diagnosis between the two periods of time. This highlights the absolute necessity of being attentive and lead a careful evaluation by haematologists but also nephrologists, cardiologists and neurologists.
Finally, according to recent studies, Daratumumab is extremely well tolerated and extremely efficient in AL amyloidosis.