THALASSAEMIA INTERNATIONAL FEDERATION

EMA Workshop on the challenges in drug development, regulation and clinical practice in Hemoglobinopathies

Patient Perspective in SCD and β-thalassemia

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Nothing to disclose

Who I am

- 61 year-old man, from Italy, married
- Graduated in “Social and Institutional Communication”; Degree on “Human Rights” (UNIGE) and in “Medicine Research and Development” (EUPATI);
- More than 40 years as patients’ advocate;
- Funding member of: Associazione Ligure Thalassemici (ALT, 1983), Thalassaemia International Federation (TIF, 1986), UNITED (Italian Federation of Patients’ Associations, 2012); IAAC (Italian Associations Advocacy Council, 2016);
- EMA: COMP member from 2018 to 2021; currently in PCWP
- EBN: member of the Governance and ePAG of the Subnetwork on RBC Defects
- Diagnosed for β-Thalassemia major at 3.5 years
- Have had more than 2000 blood units
- Splenectomy at 14, cholecystectomy at 20, kidney tumour resection at 60;

I went through the whole history of Thalassemia since when it was a fatal disease in childhood from the open prognosis nowadays

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Born in late 50s, early 60s meant:

- To be diagnosed late (unknown disease almost wherever in EU);
- To have a short life expectation (late childhood, adolescence);
- To suffer from anemia's induced complications (bone deformities, growth retard);
- To be treated only with blood transfusions (disease mechanisms almost unknown) and frequent hospitalizations;
- Many days lost at school and education seriously compromised (be proficient in the study)
- Children felt themselves diverse for the signs of the disease (facial bone deformities, short stature, poor QoL) therefore with a low grade of social integration
- Overprotection of the affected child, tricky social integration;

First breakthrough in Thalassemia (middle ‘70s)

- Improvement of disease comprehension (scientific advances);
- Day Hospital care was established (reduced hospitalizations);
- Iron overload was highlighted as an issue for the patients, that compromised the lifespan (heart failure);
- The availability of the **first drug for reducing iron burden** was the real breakthrough in the treatment of Thalassemia;
- Treatment was challenging (10 h/day by a subcutaneous infusion, through an infusion pump, 6 or 7 days a week), few patients did accept it;
- Poor compliance resulted in deaths for heart failure;

Second breakthrough in Thalassemia (middle ‘80s - early ‘90s)

- First approaches to BMT (promise for a curative treatment);
- Prenatal diagnosis (improved the prevention programs, encourage families to have healthy children);
- The availability of the **first oral drug for reducing iron burden** was the **second breakthrough** in the treatment of Thalassemia (late ‘90ies);
- Easier to take and better results in treatment adherence meant a slow but continuous drop of premature deaths;
- New technologies for imaging and **multidisciplinary approach** were paramount for the management of the disease and for preventing complications;

Nowadays

- In many EU and developed countries, excellent Standard of Care, increased lifespan and QoL for patients (only 7% of the global thalassemia population has access to the SoC); Source: Global Thalassemia Review, TIF, 2023
- Significant improvement in technology allow for a better and safer blood transfusion therapy; availability of iron chelator agents, to reduce iron overload; multidisciplinary care for monitoring and timely tackling the complications;
- Result in a dramatic change of prognosis, now thal patients can live over 60 (the average age of TDT in EU is around 45 years) Source: Global Thalassemia Review, TIF, 2023
- First Gene Therapies and ATMPs products to cure the hemolgobinopathies, low access due to high prices;

Open Access Full Text Article

ORIGINAL RESEARCH

Changes in the quality of life of people with thalassemia major between 2001 and 2009

This article was published in the following Dove Press journal:
Patient Preference and Adherence
19 March 2013
Number of times this article has been viewed

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Background: The prolonged survival of patients with thalassemia major as a result of the novel therapeutic strategies introduced in the last decade makes patient quality of life an important issue. This study investigated the changes occurring in overall quality of life in patients with thalassemia in the last decade.

Methods: This was a population-based cross-sectional survey of quality of life in the entire population with thalassemia major resident in the Liguria region of Italy from 2001 to 2009. The self-administered Short Form-36 (SF-36) questionnaire was used to measure quality of life in patients with thalassemia.

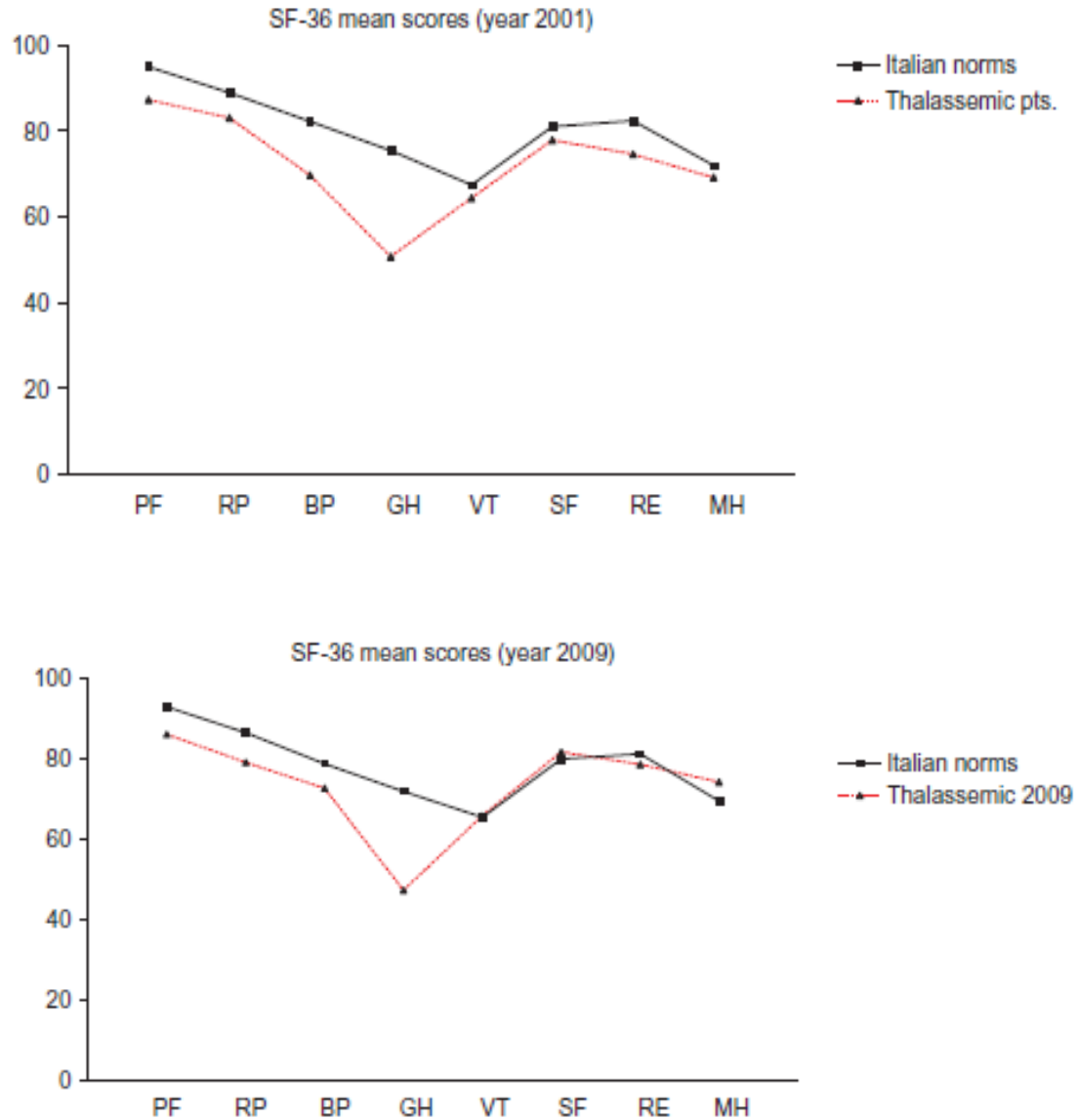
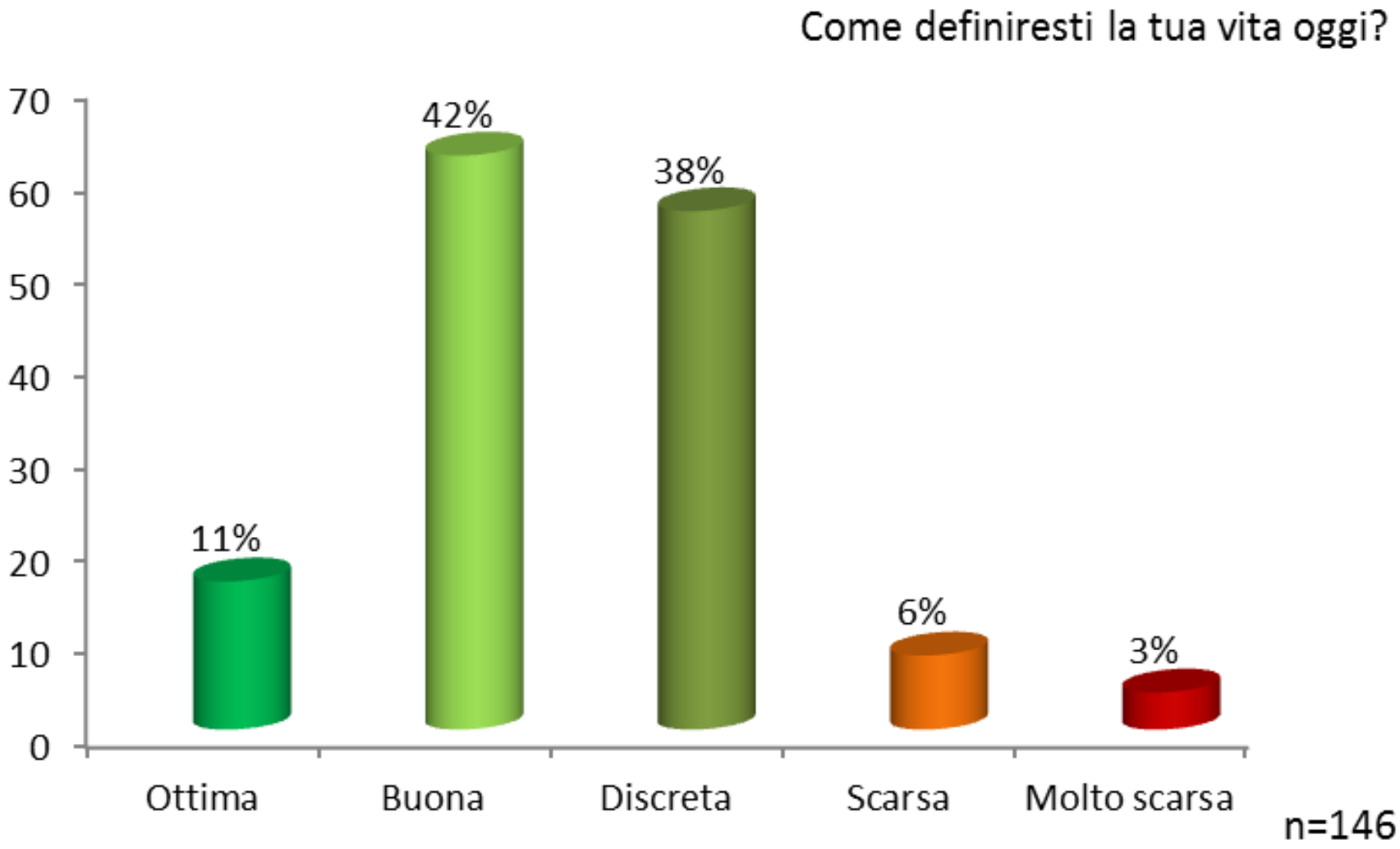


Figure 1 Quality of life profile for patients with thalassemia in 2001 (**A**) and 2009 (**B**).
Notes: Data are presented as the mean score for the population of patients with thalassemia and of the corresponding (for gender and age) normative Italian population. For each 0–100 scale, higher scores indicate better health.
Abbreviations: PF, physical functioning; RP, role-physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role-emotional; MH, mental health.


Come definiresti la tua vita oggi?
70
60
50
40
30
20
10
0
11%
42%
38%
6%
3%
Ottima
Buona
Discreta
Scarsa
Molto scarsa
n=146

Disease burden – Unmet medical needs

- Blood Transfusion is still a concern for patients; Products for increasing Hb level are welcomed if they are relevant in reducing the transfusion burden and can be self administered. A minimal increase is not significant for severe genotypes, specially if SARs can occur. Most relevant outcomes in NTDT;
- Oral Iron chelating agents are available, but more options would be needed, possibly with low number of daily administration and less side effects;
- Osteoporosis should be better addressed and prevented; many drugs to tackle it seem not to be so effective. Tackling better the Osteoporosis would mean to have a better response to pain and emerging issue in Thal;
- Multidisciplinary approach must be improved and available in all treating centers;

Disease burden – Unmet patient needs

- Younger generation of patients like to have an active life, they expect to reduce the time in hospital, to be driven towards a better nutrition and calorie intake, to became performant in sport and daily activities;
- Pain is an issue for older patients that impacts on everyday life and reduces significantly productivity at work (in 165 UK patients, 62.4% reported severe pain); Source: A.Grewal & al, Prevalence, Severity and Determinants of Pain in Thalassemia; Hemoglobin, 2023
- Mental health and lifestyle; Holistic approach is needed thinking “out of the box”
- Patients’ wealth in ageing;
- QoL measurements needs to be re-assessed with the patients’ involvement;
- PROMs, PROs, PED, RWE, should be seriously considered during the decision-making process and included in the evaluation of products.

COMP Experience (2018 – 2021)

- 12 dossiers for initial Orphan Designation of products for Hemoglobinopathies and other Rare Anemias (PKD, BDA);
- 2 dossier for products for SCD and Thalassemia at the time of MA;
- Several PA procedures and SA for products for Hemoglobinopathies;

- PROs collected in CTs rarely have been considered to be included in the evaluation due to the risk of bias or for lack of validation;
- Given the great difference of clinical phenotypes in Thalassemia and SCD, the population recruited for CTs may influence the outcomes;
- A more update definition of TDT and NTDT would be welcomed;

COMP Experience (2018 – 2021)

Limited range of drug treatments for thalassemia and Sickle cell disease

Sickle cell disease:

- **Hydroxyurea:** seems the most convincing medicine for reduction in complications and the wider used;
- **Crizalinzumab:** modest variable benefits (withdrawn for Market) and **L-glutamine** in reducing pain;
- **Voxelotor**: Consistent increase in hemoglobin but clinical benefits unclear;

Thalassemia:

- **Luspatercept**: Moderate increase in hemoglobin in more severe genotype (β0/ β0) effective in NTDT with Hb increase >1 g/dl;
- **Mitapivat**: still in CTs, for TDT; preliminary results suggest good outcomes for NTDT.

COMP Experience (2018 – 2021)

Gene Therapies for Hemoglobinopathies:

- **Zynteglo:** licensed in EU for Thalassemia with non- β0/ β0 genotype in patients 12 yo or older, in June 2019**,** withdrawn due to financial issues, no longer available in EU;
- **Casgevy**: licensed for EC in February 2024 for Thalassemia and SCD, still in negotiation in EU countries;

Concerns:

Conditioning or cytotoxic treatment; Fertility; Long-term effect; Insertional issues, developing of malignancies; Inclusion/Exclusion criteria; High cost (how many will benefit?)

Benefits:

One-time curative administration; HbF increase (Casgevy) for achieving Transfusion Independence;

Patient Preferences, PED and PROs are key to understand what patients want and how they cope with their condition

- Individuals with the exact same health status, diagnosis, or disease may have different objective observations about how they feel and function and what they prefer!

- Patient Evidence Data (PED) is essential to understand patient perspectives about the good, the bad and the ugly;

- Many surveys about QoL have been conducted without any patient involvement, only according to what the outside world (physicians, psychologists) thought it matters to the patient.

- Drafting a survey to gather data about QoL in patients with haemoglobin disorders needs to have expert patients included, otherwise outcomes can be not relevant.

Conclusions

- Hemoglobinopathies are better known and better treated but still with unmet needs.
- Some products are available for both Thalassemia and Sickle-Cell Disease but with a partial response to unmet medical needs.
- A holistic approach is needed to address secondary complication of the diseases.
- The new pharma legislation aims to push the development of medicines for rare and ultra rare diseases introducing the definition of “high unmet medical needs” and “unmet medical needs” hope that this distinct definitions will not hamper the future development of medicines for those conditions with products available.
- Innovative products and GTs have a high cost and limited access for patients even in some countries of the EU, during the negotiation an early involvement of patients would be a key to consider that burden of the disease is carefully addressed and what matter to patients.

Innovation can’t become a privilege for some instead of a right for all.

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Thank you

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