



Results of a study evaluating patient's perception regarding their erythropoiesis stimulating agent treatment in chronic kidney disease using a choice based conjoint analysis

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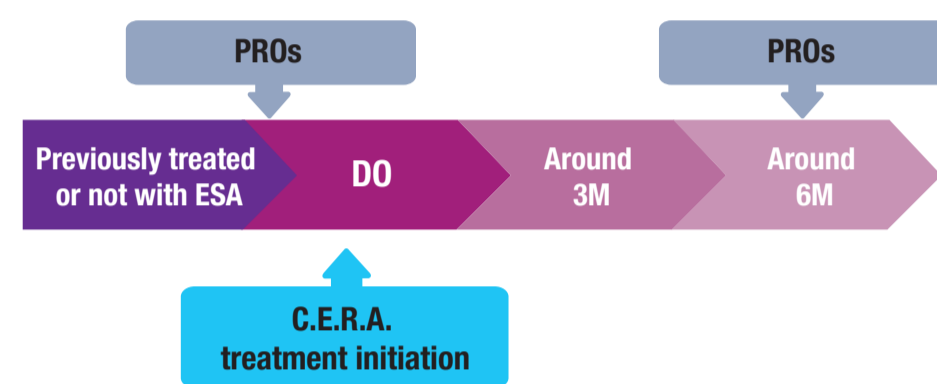
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INTRODUCTION

- Patient's perception regarding their treatment has a real interest in healthcare, especially in chronic disease. Quality of care and its improvement become an increasingly important domain in medicine and in nephrology. A growing interest emerge for patients' perception of treatment they received, in terms of preference and satisfaction.
- Patients' satisfaction with care is a major dimension of quality of care, thereby considered by healthcare authorities as a key indicator of health state [1,2], and also by many Anaemia working groups [3,4]. Patients' satisfaction with medication is a component of patients' satisfaction with care.
- The Non-Interventional Study PERCEPOLIS was conducted in France to provide data on Chronic Kidney Disease patients Not on Dialysis (CKD-ND) regarding the perception and preference they give to their Erythropoiesis-Stimulating Agents (ESA) treatment.

STUDY DESIGN

- PERCEPOLIS was a 6 months French multicentre Non-Interventional Study (NIS).
- Patients with symptomatic anemia associated with chronic kidney disease not on dialysis initiating C.E.R.A. were included between June and October 2011 by 107 nephrologists.
- PROs were collected at baseline and after 6 month of C.E.R.A. treatment.
- Clinical data were collected at baseline and every three months.



STUDY OBJECTIVES

Primary objective

- To describe in patients with chronic kidney disease not on dialysis, what characterize the preferences for an erythropoiesis stimulating agent, before and 6 months after initiation of C.E.R.A.

Secondary objectives:

- To describe patients' characteristics
- To describe utilization patterns and patients' adherence
- To evaluate the effectiveness of C.E.R.A.
- To describe the safety profile of C.E.R.A.

PATIENTS

Inclusion criteria

- Adult (≥ 18 years).
- With chronic kidney disease not on dialysis (including kidney transplant patients)
- With symptomatic anemia treated or not treated with ESA
- For whom the physician has decided prior to the study to implement a treatment with C.E.R.A.
- Patient receiving the first injection of C.E.R.A. at the inclusion visit
- Patient accepting and able to complete the questionnaire of conjoint analysis
- Patient having been informed orally and having given oral agreement for personal data to be collected and analyzed.

Non-inclusion criteria

- Current participation in a clinical trial
- Treatment with C.E.R.A. during the three months prior the study
- Planned dialysis in the next 6 months after initiation of C.E.R.A.

CHOICE-BASED CONJOINT (CBC) DESIGN

Assessment of patient preferences was developed using a discrete choice-based conjoint analysis questionnaire with the following hypothesis:

- Seven relevant characteristics (or attributes) of ESA, found on available literature:
 - Frequency of injections: 3 levels (or alternatives),
 - Contact with the healthcare practitioner/nurse : 2 levels,
 - Treatment effectiveness: 2 levels,
 - Keeping the Hb level inside the recommended target range: 2 levels,
 - Pain at injection site: 2 levels,
 - Delivery device: 3 levels,
 - Maximum period of storage at room temperature: 2 levels.
- Each possible answer includes 1 level for 2 characteristics,
- Two choices per question (including 2 attributes per choice / 1 level per attribute),
- Seven questions per CBC questionnaire.

Some constraints were used to design questionnaires to avoid impossible mix of attribute/level in the same question.

Twenty CBC questionnaires have been generated by the Sawtooth software module SSI Web version 7.0.6 in order to mix each ESA characteristics with each level. Each patient only had to answer one questionnaire.

The 20 questionnaires were equally distributed using a randomization process [5] in order to have the same number of questionnaires in each sub-population of patients previously treated or not with an ESA.

STATISTICAL CONSIDERATIONS

Primary endpoint

The primary endpoint was the relative importance according by the patient preference to different characteristics of ESA treatments before and six months after initiation of C.E.R.A.

Justification of Sample Size

Sample size calculation was based on number of attributes, number of alternatives and number of tasks.

The following rule has been used [6]:

$$n \geq \frac{t \cdot a}{c} > 1000$$

where: **n** is the number of respondents, **t** is the number of tasks, **a** is number of alternatives per task, and **c** is the number of "analysis" cells (the largest number of levels in any one attribute when considering the main effect).

Hypothesis:

Each choice task includes 2 concepts (alternatives per task) and 7 attributes

Number of levels : 3 for 2 attributes et 2 for 5 attributes (288 combinations)

Number of tasks: 5

For 600 evaluable patients : $600 \cdot 5 \cdot 2 / 3 = 2000$ representation per main effect level.

From previous NIS studies with PRO, we estimated that 20% of patients would not answer PRO or prematurely discontinue the study. Therefore around 800 patients have to be included in the study.

All analysis have been performed by subgroup of patients previously treated or not with an ESA.

DATA COLLECTION

As PRO was the primary endpoint of this NIS, it was essential to retrieve a maximum of questionnaires.

While randomization and data collection have been collected using an electronic case report form (eCRF), PROs have been performed using a Tablet PC connected to the eCRF.

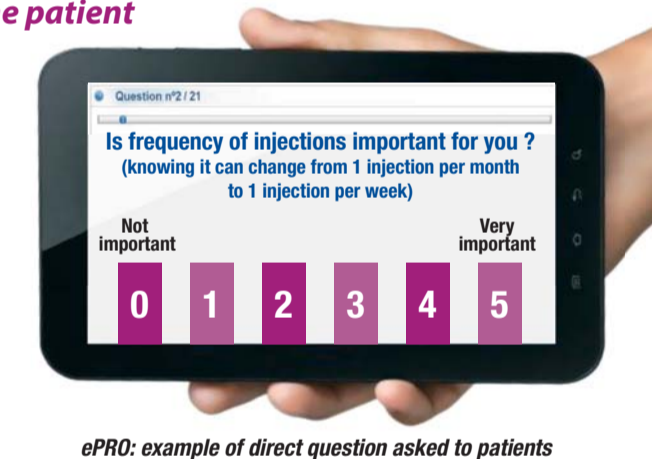


PROs ANALYSIS METHODS

Importance of each attribute declared by the patient

Each patient had to rate each characteristic: Importance declared was described in percentage per characteristic.

Each patient had to choose the most important characteristic: The most important characteristic for patients was described in percentage.



ePRO: example of direct question asked to patients

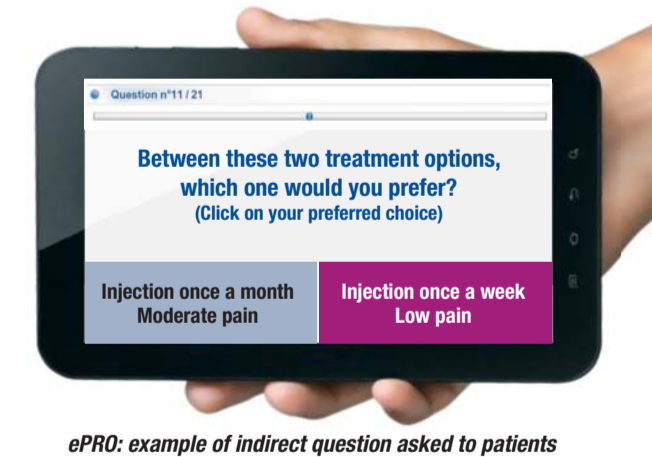
CBC questionnaire: calculated importance of each attribute

Within each questionnaire there was one fixed question that allowed to validate answers given by patients. If worst case scenario was answered to this question, the questionnaire was considered as not valid.

Analysis software and method: The analysis of preference and weight of each attribute has been performed by the Sawtooth software using hierarchical Bayesian (HB) estimation (CBC/HB module version 5.2.2.).

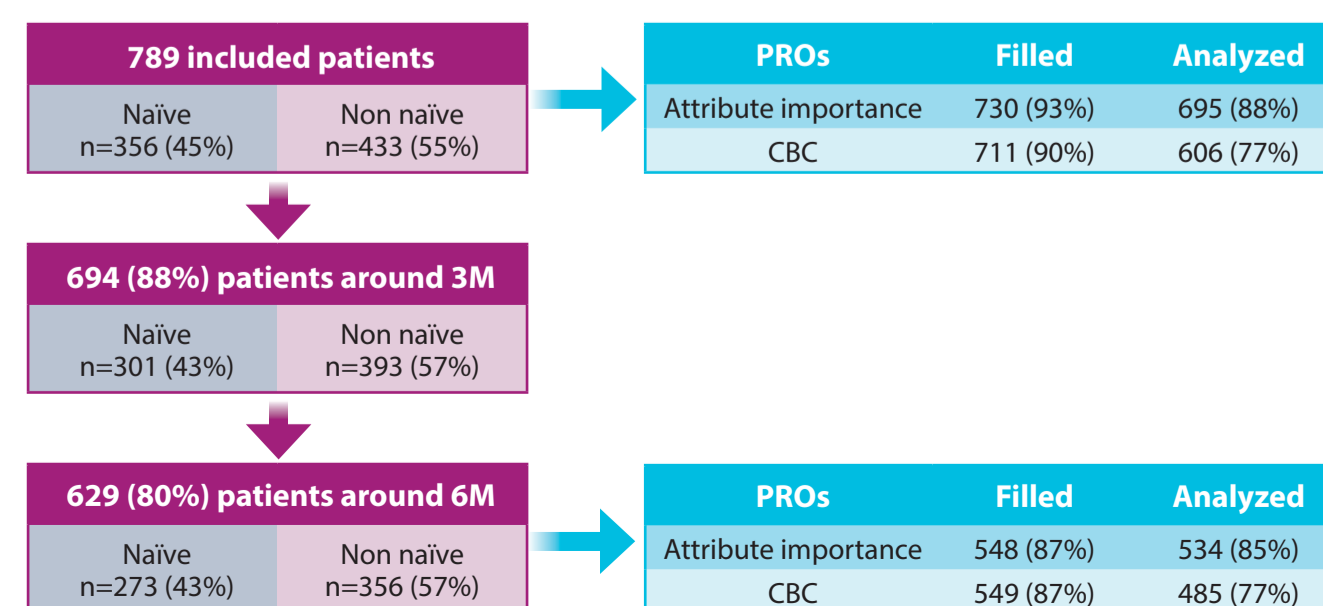
Sawtooth software has provided the following results at inclusion and around 6M:

- Individual's part worths,
- Average Utility Values,
- Average importance of each attribute.



ePRO: example of indirect question asked to patients (CBC questionnaire)

FLOW CHART



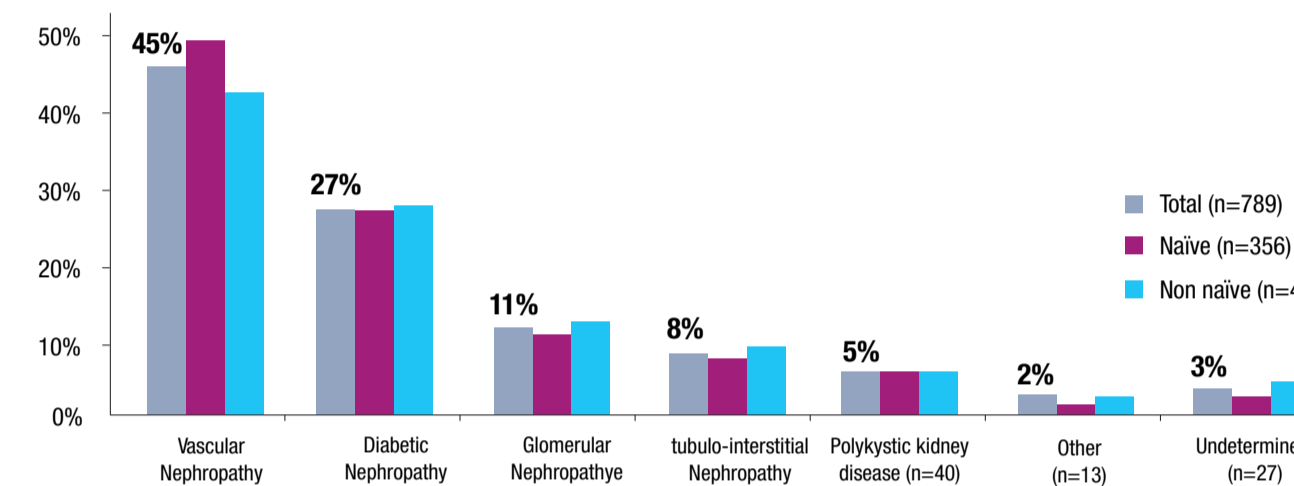
RESULTS

Baseline characteristics

	ESA naïve patients (n=356)	Non ESA naïve patients (n=433)	Total (n=789)
Men	n (%) 193 (54%)	228 (53%)	421 (53%)
Age (years)	Mean ±SD 74 ± 13	72 ± 14	73 ± 14
BMI (kg/m ²)	Mean ±SD 27 ± 5	26 ± 6	27 ± 6
Hemoglobin (g/dL)	Mean ±SD 10,0 ± 0,9	11,1 ± 1,2	10,6 ± 1,2
Simplified MDRD eGFR (ml/min/1.73m ²)	Mean ±SD 26,0 ± 10,8	25,6 ± 11,2	25,8 ± 11,0

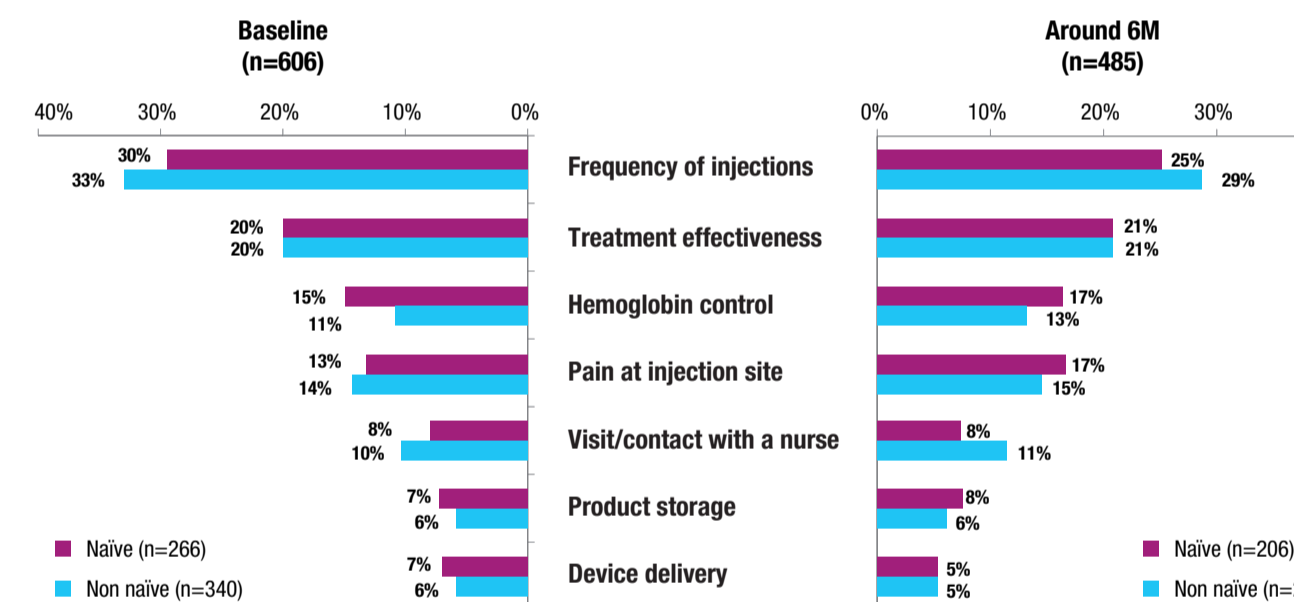
Cause of Chronic Kidney Disease (CKD)

The main cause of CKD was the vascular nephropathy followed by diabetic nephropathy.



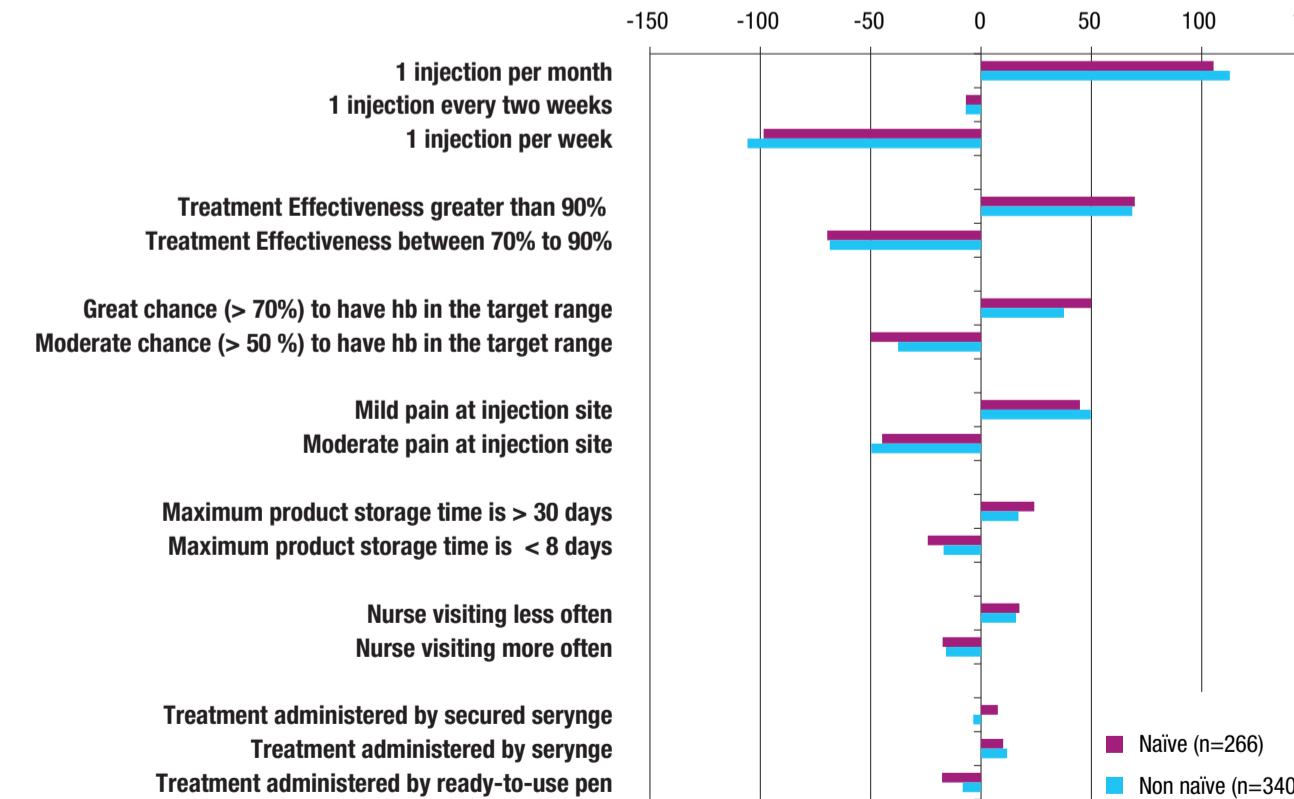
Primary analysis results: Mean importance calculated by CBC

The most important characteristic was the planned frequency of administration for around 30% of patients at baseline, followed by the importance of the treatment effectiveness for around 20%, the pain at injection site for around 14%. No major difference was found between naïve and non-naïve patients.



Primary analysis results: Mean utilities per characteristic/level at Baseline

Preference of patients goes to one injection per month, with a high treatment effectiveness, a better chance to have hemoglobin level in the target range with the lowest pain at injection site. Same utilities were found after 6 months of treatment with C.E.R.A.

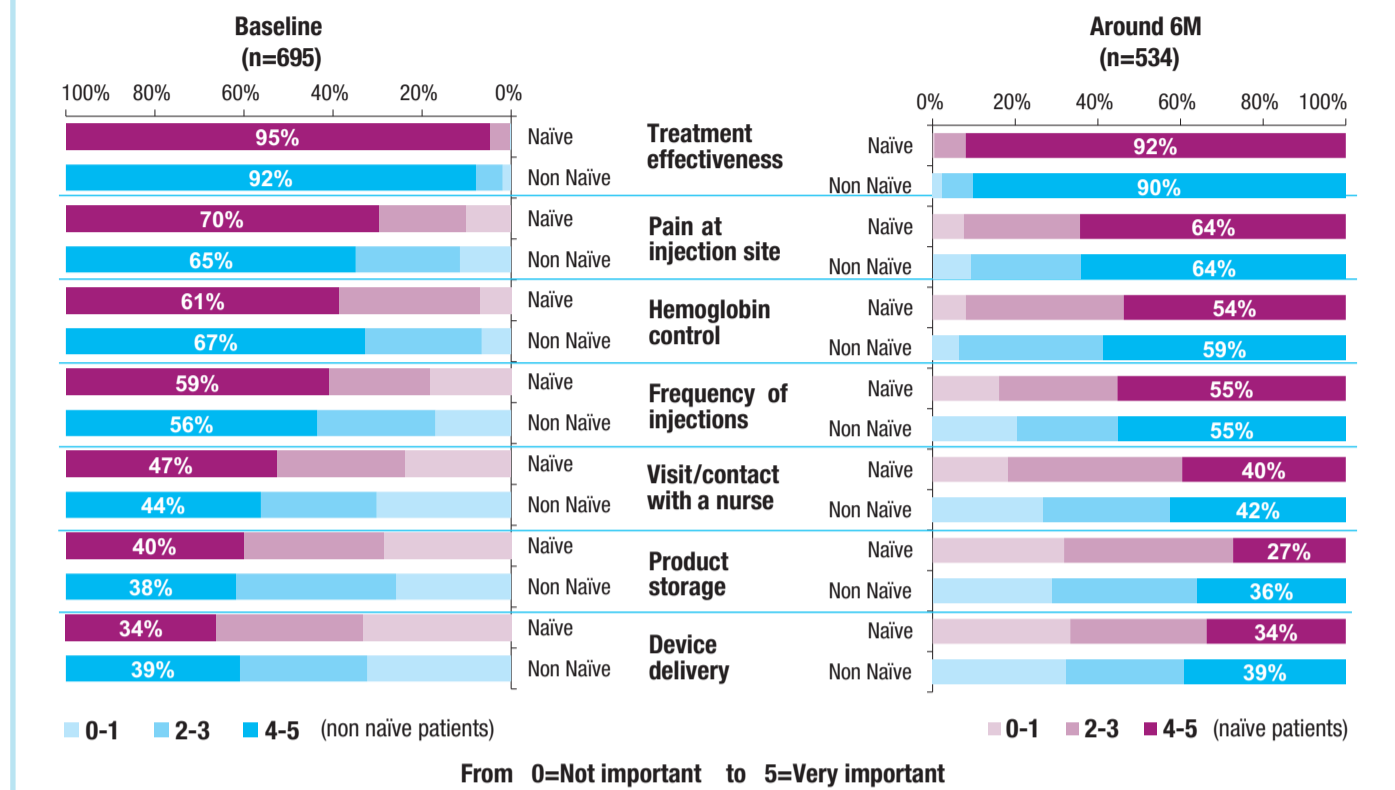


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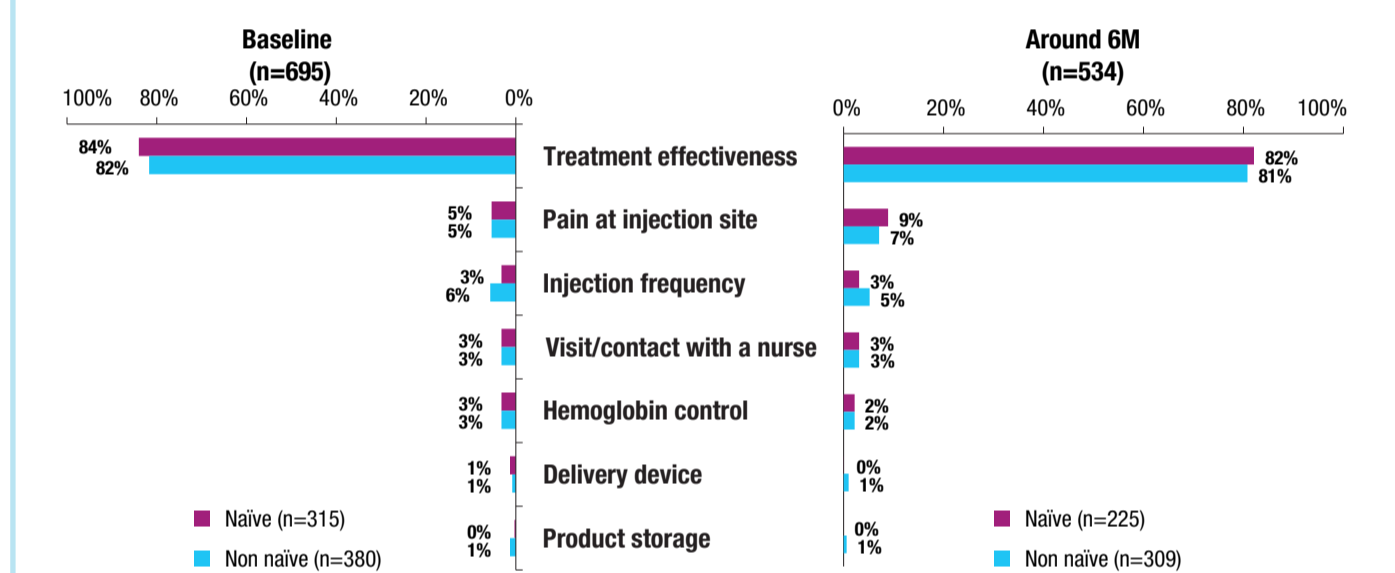
Primary analysis results : Importance of ESA characteristics declared by patients

When asking patient to rate (from 0 to 5) importance of each characteristic, the most important characteristics (>50%) are treatment efficacy, pain at injection site, having an hemoglobin level within the target range and the frequency of injection.

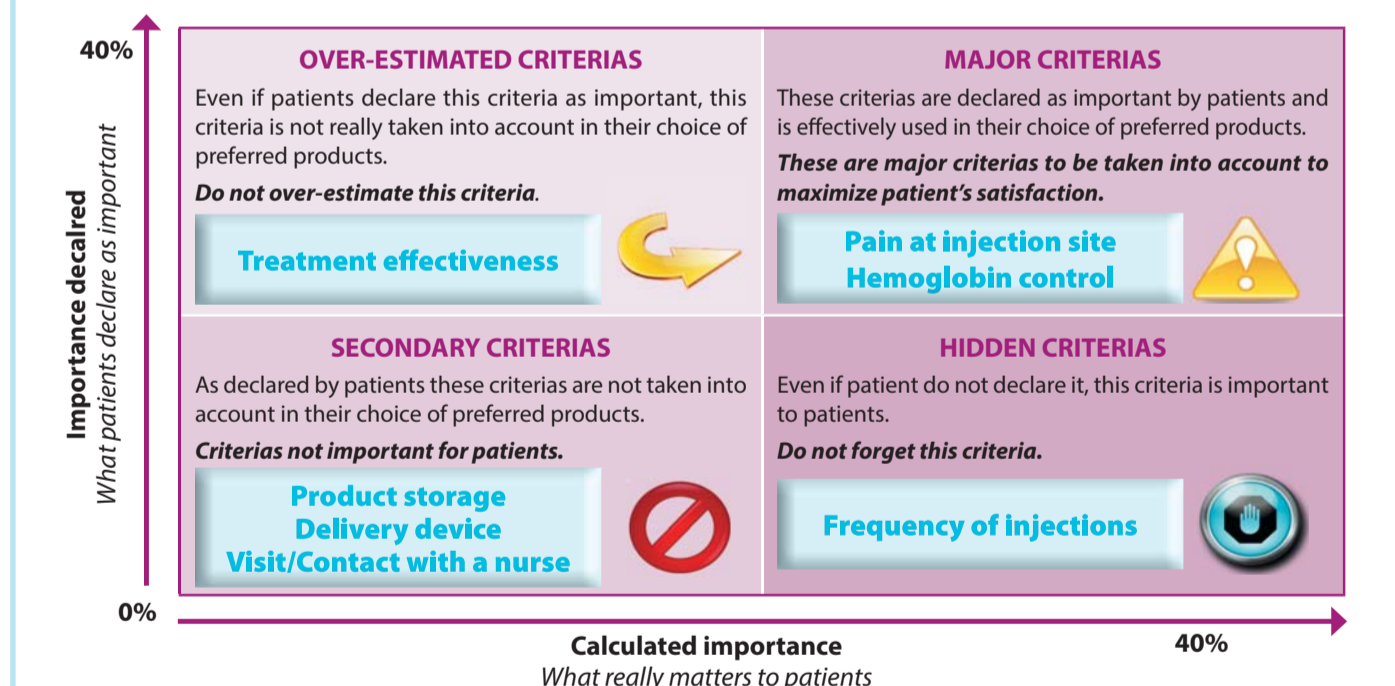


Primary analysis results: The most important characteristic declared by patient

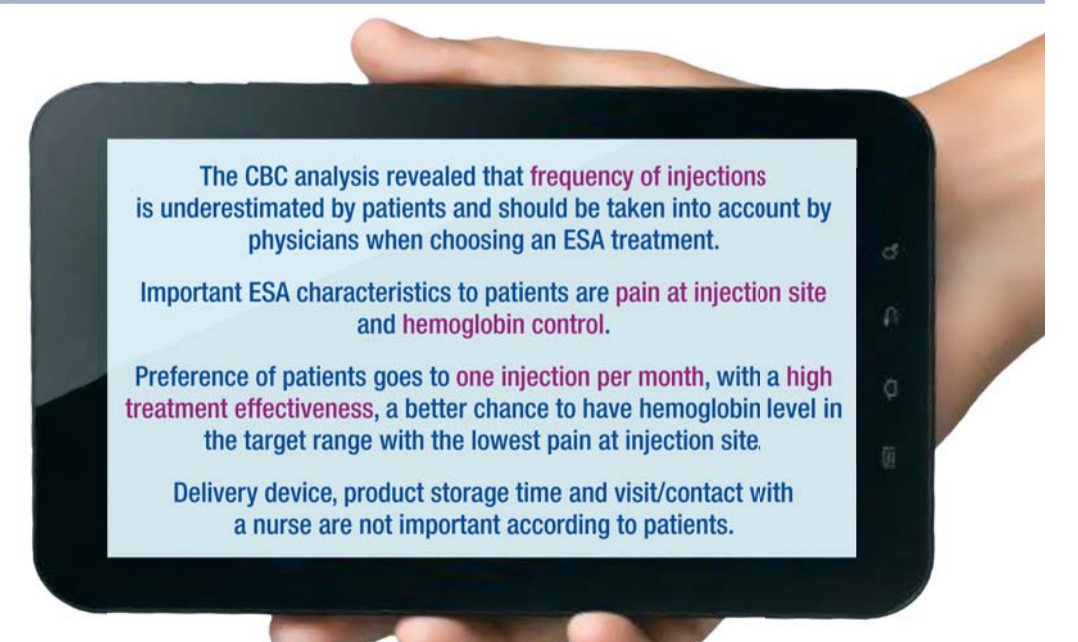
When asking a direct question to patient on which characteristic was the most important, more than 80% of them answered treatment effectiveness.



Primary analysis results : preference declared and calculated by CBC



CONCLUSION



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