UNIVERSITÀ DEGLI STUDI DI PADOVA

PROJECT

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1) Project title

Do New Biologics Improve Seminal Parameters In Male Psoriatic Patients?

2) Abstract (max 500 words)

Psoriasis is an inflammatory systemic chronic disease with an uncertain impact on male infertility; in fact, it is still unclear if the disease itself, the anti-psoriatic therapies or both may affect semen quality. Currently, I am involved in writing a systematic review about semen quality in psoriatic patients, finding few studies investigating the biological impact of different therapy on semen quality, such as retinoid derivatives (n=3), metrotrexate (MTX, n=3), TNF-inhibitors (n=1) and fumaric acid derivatives (n=1) [1-8]. Although both MTX and retinoids seem to have a detrimental effect on male fertility, international and national guidelines do not suggest sperm cryopreservation to psoriatic patients willing to have children. Noteworthy, patients are currently considered therapy free after 4 weeks from the interruption, but it is well-known that anti-psoriatic drugs need more time to be completely cleared. Therefore, the real impact of psoriasis on the seminal parameters is still not unclear. Furthermore, new classes of anti-psoriatic patients targeted IL-17 and IL-23 have revolutionized patients' expectations, since almost 90% of them achieves Psoriasis Area Severity Index (PASI) 100 at 32 weeks. Since these new biologics become extremely popular among young patients, their impact on fertility has to be further elucidated.

2.0. OBJECTIVES

•To evaluate semen quality in psoriatic patients at the baseline (T0, therapy-free)

•To evaluate the modification of semen parameters in psoriatic patients undergoing secukinumab, ixekizumab, guselkumab and risakizumab after 12 (T1), 24 (T2),36 (T3), 52 (T4) weeks, 104 weeks (T5).

3.0. STUDY DURATION: 6 months enrolment, 2 years follow-up, 6 months analysis

4.0. STUDY DESIGN

We will perform a multicenter prospective pilot study assessing 80 adult (>18 years) plaque psoriasis patients undergoing secukinumab, ixekizumab, guselkumab and risakizumab (20+20+20+20) to the approved dosage. Three Italian primary referral centers will be involved in this project: IRCCS Istituto

Ortopedico Galeazzi (cohort: 340 patients), IRCCS San Donato (cohort: 1193 patients), IRCCS San Gallicano (cohort: 800 pateints). Ethical Committee of each center will verify the study protocol in compliance with Declaration of Helsinki. All patients will sign a written consent. Patients will be examined by two independent board certified dermatologists that will collect medical history, demographics and pharmacological history. During dermatological assessment, psoriatic patients will undergo Psoriasis Area Severity Index (PASI), Dermatologic Life Quality Index (DLQI) and Psoriasis Epidemiology Screening Tool (PEST). In case the PEST suggests a possible psoriatic arthritis, they will additionally undergo Classification criteria for Psoriatic Arthritis (CASPAR) and Disease Activity in Psoriatic Arthritis (DAPSA). Semen parameters will be evaluated at the baseline and after 12, 24, 36, 52 and 104 weeks, following the WHO guidelines 5th edition (WHO, 2010) [9,10].

4.1. ENROLMENT

Inclusion criteria: i) adult (>18 years but <65 years) patients with moderate-to-severe (PASI >10) plaque psoriasis starting monotherapy with secukinumab, or ixekizumab, or guselkumab or risakizumab and following the approved dosage, ii) psoriasis duration >5 years, iii) availability of diet, demographic and medical data iv) absence of malignancy or malignancy occurred.

Exclusion criteria: i) pediatric (<18 years) or elder > 65 years patients, ii) different type of psoriasis from plaque, iii) following vegetarian/vegan diets or other special diet (i.e. paleolitic, ketogenic, intermittent circadian fasting), iv) smokers (>1 cigarette in 1 month) or ex-smokers from less than 10 years (included vapers), v) addictions (alcohol AUDIT>7, abuse of marjuana or other drugs), vi) presence of acute and chronic infections, autoimmune and inflammatory comorbidities, varicocele or other urinary acquired or congenital abnormalities, vii) consumption of secukinumab, or ixekizumab, or guselkumab or risakizumab non in monotherapy.

4.2. SEMINAL PARAMETERS

The following semen parameters will be evaluated by a trained operator according to the most recent WHO guidelines (5th edition, 2010): semen volume, pH, sperm concentration and total sperm count, , total motility (progressive and non-progressive), morphology and vitality. The presence of leukocytospermia (seminal leukocyte >1million/ml) will be assessed by the Endtz test. In case of sperm agglutination, the presence of anti-sperm antibodies will be tested. Moreover, the Male Infertility Oxidative System (MiOXSYS) will be used to assess oxidation-reduction potential (ORP) as a new marker of seminal DNA fragmentation [10].

4.3. FEASIBILITY

Available cohort of 2333 patients under biologics in which 500 under secukinumab, or ixekizumab, or guselkumab or risakizumab. Spontaneous study sponsored by industry.

Collaborators:

-Prof Ashok Agarwal from the American Center for Reproductive Medicine, Cleveland Clinic, Cleveland, OH, USA (male infertility)

-Dr Concetta Iovine from the Italian Center for Reproductive Medicine, Naples, Italy (MiOXSYS device)

-Prof Enzo Grossi from Villa Santa Maria Institute, Via IV Novembre Tavernerio, 22038, Como, Italy (Machine Learning patented programs)

5.0. ANALYSIS Linear and non-linear statistics (machine learning supervised (TWIST) and unsurpevised (AutoCM)) [11,12]