Prevention of dysbiosis complications with autologous fecal microbiota transplantation (auto-FMT) in AML patients undergoing intensive treatment (ODYSSEE study): First results of a prospective multicenter trial

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INTRODUCTION

The microbiota plays a significant role in human health and disease, particularly in shaping the gut immune cell responses, thereby altering host susceptibility to inflammation and infection at sites of colonization.

Many cancer therapies lead to an inflammatory condition such as mucositis, associated with gut barrier deterioration and bacterial translocation. These drugs also cause neutropenia, bacterial translocation across the gut mucosa, also leading to severe systemic infections that will require antibiotics. Intensive treatments of Acute Myeloid Leukemia (AML) are known to negatively impact gut microbiota composition, measured by a deep shutdown of diversity indices (eg. Simpson), also called dysbiotics.

Therefore, development of strategies to manipulate the gut microbiota may minimize treatment-related complications and potentially improve outcomes.

We propose to use autologous transplantation of fecal microbiota to AML patients treated with intensive chemotherapy and antibiotics in order to restore the balance of their intestinal microbiota.

STUDY DESIGN AND PATIENTS

STUDY OBJECTIVES

Main Objectives:

Primary: Recovery of microbiota diversity and correction of dysbiosis after auto-FMT

Secondary:

Safety and feasibility of auto-FMT

Impact of auto-FMT on several patient-related outcomes (clinical status, immune status and recovery)

Exploratory assessment of a dysbiosis biomarker

Key Inclusion Criteria

≥ 18 and ≤ 75 years old

de novo diagnosis of AML

Intensive chemotherapy (*3-F or equivalent)

Antibiotics 2 days at V1

Detection of resistant or pathogenic bacteria, parasites, viruses in feces at V1

Severe colitis or digestive disorders within 3 months before V1

Demographics and Baseline Characteristics

35 AML eligible screened patients

9 patients fulfilling all inclusion criteria inclusion and treated with auto-FMT, presented in this interim analysis

Ages: yrs; median (range) 47 (20-67)

Gender, n (%)

35 AML eligible screened patients

9 patients fulfilling all inclusion criteria inclusion and treated with auto-FMT, presented in this interim analysis

RESULTS

Microbiome Summary

- Huge impact of chemotherapy/antibiotics on microbiome diversity at genus level (idem species level, data not shown)

- Total recovery of microbiota diversity after auto-FMT

- Significant increase of the antibiotic resistance gene copynumbers after chemotherapy/antibiotics, returned to baseline after auto-FMT

METHODS - STUDY FLOW CHART

- Inoculum manufactured under GMP conditions

安全 Summary

- Auto-FMT well tolerated

- 1 serious adverse event post-FMT reported (E. coli infection resolved after appropriate antibiotic therapy)

CONCLUSIONS

This first multicenter prospective trial reached its primary endpoint in all analyzed cases thus far, and established the feasibility of auto-FMT to correct dysbiosis and restore a normal microbiota in AML patients receiving intensive induction chemotherapy and wide-spectrum antibiotics. Clinical, biochemical and immunological parameters of this interim analysis are currently being analyzed and suggest correlation between microbiota restoration and clinical outcomes such as infection-related complications, sequelae to the gastrointestinal tract as well as other co morbidity factors in order to improve the overall mortality of the disease.