Protocol Title: THE EFFICACY AND SAFETY OF LENALIDOMIDE (Revlimid®) MONOTHERAPY IN RED BLOOD CELL TRANSFUSION DEPENDENT SUBJECTS WITH MYELODYSPLASTIC SYNDROME ASSOCIATED WITH A DEL (5q) CYTOGENETIC ABNORMALITY

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BACKGROUND AND RATIONALE

The myelodysplastic syndromes (MDS) are a group of disorders in which there is failure of the bone marrow to produce adequate circulating blood cells leading to a low haemoglobin (anaemia), a low white cell count (neutropenia) and a low platelet count (thrombocytopenia). In some patients there is also an excess of immature cells (blasts) and transformation into leukaemia can occur. A small proportion of patients with MDS demonstrate an abnormality of chromosome 5, in which a small portion is deleted. This abnormality is associated with a specific subtype of MDS, the 5q- syndrome. Patients with the 5q- syndrome have a refractory anaemia, may be transfusion dependent and have a median survival of approximately 5 years. There has been no effective therapy to date and treatment consists of regular blood transfusions and its associated complications.

Lenalidomide (Revlimid®) is an oral drug related to thalidomide and is a member of a class of drugs known as immunomodulatory drugs (IMiDs). IMiDs have activity in MDS. lenalidomide (Revlimid®) has a potentially greater potency than thalidomide (5-2000X) and has been demonstrated to be safe with differing adverse effects compared with thalidomide. In early studies of lenalidomide (Revlimid®) in all MDS patients, up to 56% showed a response by becoming less anaemic and requiring less or no further blood transfusions. In addition, 100% of patients with the 5q- abnormality achieved a complete cytogenetic remission and up to 86% of transfusion dependent patients with the 5q- abnormality can become transfusion independent. It is currently undergoing licensing studies in the US.

Existing data suggested that lenalidomide (Revlimid®) may be especially active in patients with the 5q- abnormality. The actual mechanism through which lenalidomide (Revlimid®) exerts its effects is not known. Given the rarity of the 5q- syndrome, it would be important to maximise our understanding of the mechanism by which this abnormality affects bone marrow cells and the effect that lenalidomide exerts upon this.

TRIAL OBJECTIVES

Primary:

To evaluate the efficacy of lenalidomide treatments to achieve haematopoietic improvement in subjects with low- or intermediate-1 risk International Prognostic Scoring System[1] (IPSS) myelodysplastic syndrome (MDS) associated with a del 5q cytogenetic abnormality.

To evaluate the efficacy of lenalidomide to achieve haematopoietic improvement in patients with isolated del5q with blasts <20%

Secondary:

To evaluate the safety of lenalidomide treatments in MDS subjects with a del5q cytogenetic abnormality.

To attempt to determine further the genetic and cellular changes involved with the development of the 5q- syndrome and the effects of lenalidomide (Revlimid®) upon these cells.

TRIAL DESIGN

A single centre, single-arm, open-label study of oral lenalidomide monotherapy administered to red blood cell (RBC) transfusion dependent subjects with IPSS low- or intermediate-1 risk MDS associated with a del5(q) cytogenetic abnormality and also in patients with isolated del5q with blasts <20%.To evaluate the efficacy of lenalidomide treatments to achieve haematopoietic improvement in subjects with low- or intermediate-1 risk International Prognostic Scoring System1 (IPSS) myelodysplastic syndrome (MDS) associated with a del 5q cytogenetic abnormality To evaluate the efficacy of lenalidomide to achieve haematopoietic improvement in patients with isolated del5q with blasts <20%

DEMOGRAPHICS

44 participants aged 18-84 years, with myelodysplastic syndrome associated with associated with a del 5(q) cytogenetic abnormality were recruited at one clinical site, into this trial between 2005 and 2016.

Table 1 Demographic Characteristics

	Overall Trial
Number of subjects	44
AGE	
Adults (18-70 years)	25
Adults (71-80years)	15
81 years and over	4
Gender	29
Female	29
Male	15

RESULTS

Data was analysed from 36 participants who completed the trial

Table 2 Completion data

	N = Participants
Started	44
Completed	36
Not Completed	8
• Died	8

Altogether 76% of the patients showed erythroid response, 60% even reached transfusion independence in the study period. This real world data shows the efficacy of lenalidomide in spite of the observed significant toxicities, supporting the results of previously published clinical trials.

ADVERSE EVENTS

41% (18/44) participants reported a Serious Adverse Event, of these, 8 resulted in death.

85% (37/44) participants reported adverse events.