BRISTOL MYERS SQUIBB RESEARCH AND DEVELOPMENT

SUMMARY OF THE RISK MANAGEMENT PLAN FOR LENALIDOMIDE (REVLIMID®)

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Disclaimer:

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them. The RMP summary of REVLIMID® is a concise document and does not claim to be exhaustive. As the RMP is an international document, the summary might differ from the "Arzneimittelinformation / Information sur le médicament" approved and published in Switzerland, eg, by mentioning risks occurring in populations or indications not included in the Swiss authorization. Please note that the reference document which is valid and relevant for the effective and safe use of REVLIMID® in Switzerland is the "Arzneimittelinformation/ Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic. Bristol-Myers Squibb SA is fully responsible for the accuracy and correctness of the content of the published summary RMP of REVLIMID®.

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1 SUMMARY OF THE RISK MANAGEMENT PLAN

This is a summary of the risk management plan (RMP) for REVLIMID. The RMP details important risks of REVLIMID, how these risks can be minimised, and how more information will be obtained about REVLIMID 's risks and uncertainties (missing information).

REVLIMID's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how REVLIMID should be used.

This summary of the RMP for REVLIMID should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of REVLIMID's RMP.

1.1 The Medicine and What it is Used For

REVLIMID is authorised in combination with rituximab for the treatment of adult patients with previously treated follicular lymphoma (FL); as monotherapy for the maintenance treatment of adult patients with newly diagnosed multiple myeloma (NDMM) who have undergone autologous stem cell transplantation (ASCT); in combination with dexamethasone for the treatment of MM in adult patients who have received at least one prior therapy; in combination with dexamethasone, or bortezomib and dexamethasone, or melphalan and prednisone for the treatment of adult patients with previously untreated MM who are not eligible for transplant; as monotherapy for the treatment of adult patients with transfusion-dependent anaemia due to low or intermediate 1 (INT-1) risk myelodysplastic syndrome (MDS) associated with an isolated deletion 5q (del 5q) cytogenetic abnormality when other therapeutic options are insufficient or inadequate; and as monotherapy for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (RRMCL) (see SmPC for the full indication). REVLIMID contains lenalidomide as the active substance and it is given by oral route of administration.

Further information about the evaluation of REVLIMID’s benefits can be found in REVLIMID’s EPAR, including in its plain-language summary, available on the European Medicines Agency (EMA) website, under the medicine’s webpage: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/000717/human_med_001034.jsp&mid=WC0b01ac058001d124.

1.2 Risks Associated with the Medicine and Activities to Minimise or Further Characterise the Risks

Important risks of REVLIMID, together with measures to minimise such risks and the proposed studies for learning more about REVLIMID's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals
- Important advice on the medicine’s packaging

- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly
- The medicine's legal status — the way a medicine is supplied to the patient (e.g., with or without prescription) can help to minimise its risks

Together, these measures constitute *routine risk minimisation* measures.

In the case of REVLIMID, these measures are supplemented with *additional risk minimisation measures* mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including PSUR assessment, so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of REVLIMID is not yet available, it is listed under 'missing information' below.

1.2.1 List of Important Risks and Missing Information

Important risks of REVLIMID are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of REVLIMID. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (eg, on the long-term use of the medicine).

Table 1.2.1-1: List of Important Risks and Missing Information

Important identified risks	Teratogenicity
	Serious infection due to neutropenia
	Second primary malignancies (SPM)
	Tumour Flare Reaction (MCL and FL Indications)
	Cardiac failure
	Cardiac arrhythmia
	Ischaemic heart disease (including myocardial infarction)
Important potential risks	Off-label use
Missing information	None

1.2.2 Summary of Important Risks

Table 1.2.2-1: Important Identified Risks

Teratogenicity	
Evidence for linking the risk to the medicine	Lenalidomide is structurally related to thalidomide, which is known to cause serious birth defects and death of the foetus. In nonclinical studies, lenalidomide induced malformations similar to those described with thalidomide. Therefore, a teratogenic effect of lenalidomide is expected and lenalidomide is contraindicated during pregnancy.
Risk factors and risk groups	The 'at risk' group comprises females of childbearing potential (FCBP) or female partners of male patients treated with lenalidomide and there are no risk factors.

Risk minimisation measures	Routine risk minimisation activities:
	• Section 4.3 of SmPC: contraindicated in pregnant women and in FCBP unless all the conditions of the BMS PPP are met.
	• Section 4.4 of SmPC: warnings and precautions for use
	  • Criteria for women of non-childbearing potential
	  • Counselling
	  • Contraception
	  • Pregnancy testing
	  • Precautions for men
	  • Additional precautions
	  • Reference to educational materials, prescribing and dispensing restrictions.
	• Section 4.6 of SmPC: fertility, pregnancy and lactation.
	• Sections 4.8 and 5.3 of SmPC: the potential teratogenic effects of lenalidomide are highlighted.
	• Pack size:
	  • The pack is based on a maximum 4-week supply of capsules to ensure that FCBP are required to obtain a new monthly prescription with a medically supervised pregnancy test.
	Legal status: Lenalidomide is subject to restricted medical prescription.
	Additional risk minimisation measures:
	• BMS PPP
	• Educational Programme
	• Direct HCP communication prior to launch
	• Direct HCP communication with findings from CC-501-TOX-004
	• Educational HCP's kit to include: Educational Healthcare Professional brochure; Educational brochures for patients; Patient card; Risk awareness forms; Information on where to find latest SmPC
	• Therapy management
	• Criteria for determining FCBP, Contraceptive measures and pregnancy testing for FCBP
	• Advice in SmPC, Dear HCP letter and educational materials
	• System to ensure appropriate measures have been completed.

Table 1.2.2-1: Important Identified Risks

	• Patient card to document childbearing status, counselling and pregnancy testing.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • MDS-012 Additional monitoring of implementation of BMS PPP on a country specific basis in accordance with local legal framework and with agreement of the relevant NCA (ie, monitoring of patient card completion, monitoring by external agency and surveys).
Serious Infection due to Neutropenia	
Evidence for linking the risk to the medicine	In clinical trials, neutropenia has been reported as a consequence of lenalidomide treatment; ≥ Grade 3 and ≥ Grade 4 infections have occurred in the context of neutropenia (any grade).
Risk factors and risk groups	Haematologic malignancies by themselves or by virtue of their therapeutic strategies, chemotherapy, radiation or haematopoietic stem cell transplant put patients at risk of infections. The introduction of stem cell transplantation and novel anti-myeloma agents has improved the outcome of patients with MM. These advances have transformed MM into a chronic condition, with multiple relapses and salvage therapies, all of which results in cumulative immunosuppression and higher risk of infection. For example, application of stem cell transplantation has broadened the spectrum of infection to include those caused by Clostridium difficile, cytomegalovirus, and opportunistic moulds. Risk factors include myeloma-related innate immunodeficiency, which involves various arms of the immune system and includes B-cell dysfunction (manifested as hypogammaglobulinemia). Polyclonal hypogammaglobulinemia has been classically associated with infection by encapsulated bacteria, such as Streptococcus pneumoniae and Haemophilus influenzae. Myeloma and treatment-associated organ dysfunctions and comorbidities also increase the risk of infection. These dysfunctions and comorbidities include (1) renal failure (cast nephropathy, hypercalcemia, deposition disease, and others), respiratory compromise, caused by collapse of thoracic vertebra and opiate therapy (which may depress the central nervous system) given to patients with painful fractures (3) severe alimentary mucosal damage (caused by chemotherapy, radiation therapy, or graft-versus-host disease) (4) hyperglycemia induced by dexamethasone (5) transfusional iron overload and (6) the multisystem involvement by myeloma-associated deposition diseases (AL-amyloidosis and light chain deposit disease). Indeed, levels of CD4+ T cells, particularly naive and activated subsets, decrease significantly with increasing cycles of chemotherapy, a decrease strongly associated with opportunistic infections. Finally, myeloma typically affects an older population, with a median age of 62 to 73 years. These patients frequently experience an age-related decline in physiologic reserve of various organs and from other age-related conditions, including frailty, geriatric syndromes, cognitive dysfunction, and social isolation, all of which may increase the risk of infection. Lenalidomide treatment in combination with dexamethasone in MM patients with at least one prior therapy is associated with a higher incidence of Grade 4 neutropenia compared to placebo-dexamethasone treated patients (SmPC, Section 4.4). The combination of lenalidomide with melphalan and prednisone in clinical trials of NDMM patients is associated with a higher incidence of Grade 4 neutropenia than MPp+p treated patients (SmPC, Section 4.4).

Table 1.2.2-1: Important Identified Risks

	The proportion of patients who experienced Grade 3 or 4 myelosuppression in one study of lenalidomide-treated patients with MM was significantly higher for patients who had prior high-dose chemotherapy and stem cell transplantation, compared with those that did not. Impairment of antibody response, neutropenia, treatment with glucocorticoids, and reduction of normal Ig all increase the likelihood of infection. While a much greater proportion of lenalidomide/dexamethasone patients experienced neutropenia relative to placebo/dexamethasone patients, this increased risk did not translate into an infection risk of the same magnitude in either the total study population or in the study population restricted to Grade 3 or 4 toxicities. Lenalidomide treatment in MDS patients is associated with a higher incidence of Grade 3 or 4 neutropenia compared with patients on placebo (SmPC, Section 4.4). In patients with MDS, those experiencing neutropenia while receiving lenalidomide may be at increased risk for infections.
Risk minimisation measures	Routine risk minimisation measures: • Section 4.2 of SmPC: dose reduction advice for neutropenia. • Section 4.4 of SmPC: warning of neutropenia, and infection with or without neutropenia, and advice for monitoring patients, including blood testing for neutropenia. Advice that patients should report febrile episodes promptly. Advice regarding establishing HBV status before treatment, use in patients previously infected with HBV and monitoring for signs and symptoms of active HBV infection throughout therapy. • Listed as ADRs in Section 4.8 of SmPC. • Advice to patients in PL, including that the doctor is advised to check if the patient has ever had hepatitis B infection prior to starting lenalidomide treatment. Additional risk minimisation measures: • None.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Connect® MM Registry • MDS-012
SPM	
Evidence for linking the risk to the medicine	In clinical trials, AML and B-cell malignancies have been reported in patients treated with lenalidomide. Based on clinical trial data, lenalidomide may increase the risk of NMSC. Patients with MM also have an increased risk of NMSC. Patients treated with lenalidomide may be at increased risk of developing new cancers. The reason for this is not clear, but further investigations are being undertaken.
Risk factors and risk groups	**MDS Populations (Haematologic Malignancies)** A study to identify prognostic factors for progression to leukaemia (LFS) and OS was reported by Malcovati. Four hundred seventy-six patients first diagnosed with de novo MDS between 1992 and 2002 were evaluated. In one of the earliest studies to report the negative effects of developing a transfusion requirement, Malcovati reported an increased risk associated with transfusion burden when analysed as a time-dependent covariate in a combined group of patients with RA, RARS or MDS with del(5q) (HR = 3.46).

Table 1.2.2-1: Important Identified Risks

Further development of the WPSS a learning cohort of 426 Italian MDS patients and a validation cohort of 193 German MDS patients was reported by Malcovati and colleagues. In a multivariable analysis of the Italian patients stratified by WHO subgroups, cytogenetics (HR = 1.48) and transfusion requirement (HR = 2.53) significantly affected OS and risk of AML (HR = 1.3 and HR = 2.4, respectively). These findings were corroborated in the subsequent multivariable analysis of German MDS patients stratified by WHO subgroups, with cytogenetics (HR = 1.84) and transfusion dependency (HR = 1.85) and risk of AML (HR = 2.27 and HR = 2.25, respectively). Mallo reported the results of a cooperative study designed to assess prognostic factors for OS and progression to AML in 541 patients with de novo MDS and del 5q. In multivariate analyses the most important predictors of both OS and AML progression were number of chromosomal abnormalities ($p < 0.001$ for both outcomes), platelet count ($p < 0.001$ and $p = 0.001$, respectively) and proportion of bone marrow blasts ($p < 0.001$ and $p = 0.016$, respectively). Transfusion burden was not addressed in this study.

Knuendgen assessed the risk of AML progression and death in 295 lenalidomide-treated MDS-003 and MDS-004 patients versus 125 MDS patients with del 5q from a large multicentre registry who had received best supportive care only including ESAs. In the final multivariate Cox proportional hazard models, lenalidomide treatment was not associated with progression to AML (HR 0.939; $p = 0.860$). Significant factors associated with an increased risk of AML progression were complex cytogenetics (del 5q plus > 1 abn; HR 3.627; $p = 0.002$), bone marrow blasts 5% to 10% (HR 2.215; $p = 0.016$), and higher transfusion burden (HR 1.097 [10% increase in risk per unit at baseline]; $p = 0.029$). Higher haemoglobin levels were associated with a reduced risk (HR 0.857; $p = 0.054$). Regarding survival, lenalidomide treatment was associated with a reduced risk of death (HR 0.597; $p = 0.012$).

Other factors associated with decreased mortality were higher haemoglobin levels (HR 0.883; $p = 0.028$), higher platelet counts (HR 0.999; $p = 0.035$), and female sex (HR 0.598; $p = 0.002$). Higher transfusion burden (HR 1.056; $p = 0.037$) and age (HR 1.049; $p < 0.001$) increased the risk of death.

Mutations in the TP53 gene have been well described as a poor prognostic variable and associated with chemotherapy resistance in a wide variety of malignancies including high-risk MDS and AML.

MCL Population (Haematologic Malignancies)

There is no information available.

NMSC

Risk factors for NMSC include: increased sun or ultraviolet radiation exposure; physical factors such as fair skin, red or blond hair, and light eye colour; chemical carcinogens such as, arsenic, tobacco, and oral methoxsalen; ionising radiation; and previous history of NMSC.

- **Prolonged survival as a result of improved therapies**

As previously noted, the 5-year relative survival among MM patients has increased from 24.6% among patients first diagnosed in 1975 to 1977 to 44.9% among patients first diagnosed between 2003 and 2009.

Due to improvements in the care of patients with cancer, the number of cancer survivors has been increasing in recent years. Increased longevity increases the risk of developing second malignancy, including NMSC.

Table 1.2.2-1: Important Identified Risks

	• **Immunosuppression associated with transplantation procedures** Immunosuppression is a risk factor for NMSC. Patients receiving immunosuppressive therapy following solid organ transplantation and those receiving bone marrow transplants have an increased risk of skin cancer. In a small series of patients (n = 43) receiving nonmyeloablated haematopoietic cell transplants, 6 patients developed squamous cell carcinoma (n = 3), basal cell carcinoma (n = 2), or malignant melanoma (n = 2). In another study, the most frequently observed secondary malignancies among patients (n = 557) receiving allogeneic bone marrow transplants were NMSC. Out of 31 secondary malignancies, 5 were basal cell carcinoma and 4 were squamous cell carcinoma skin cancers.
Risk minimisation measures	Routine risk minimisation measures: • Section 4.4 of SmPC warning of SPM and advice for cancer screening. • Listed as ADRs in Section 4.8 of SmPC. • Advice to patients provided in PL. Additional risk minimisation measures: • Dear HCP letter. • Educational HCP brochure.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Connect® MM Registry. • MDS-012 • Connect® MDS/AML Disease Registry. • Long-term follow-up (at least 5 years from the date of the randomisation of the last patient in the study) for SPM in all BMS-sponsored clinical trials; 3 years for MDS-012 • Solicited reporting of SPM in all BMS-sponsored clinical trials (status of clinical trials will be updated with each PSUR and DSUR cycle).
Tumour Flare Reaction (MCL and FL Indications)	
Evidence for linking the risk to the medicine	Based on clinical trial data, lenalidomide may increase the risk of TFR in patients with CLL and other lymphomas.
Risk factors and risk groups	Tumour flare reaction has been associated with greater tumour burden in CLL In Study MCL-002, in the final multivariate model, high MIPI score at diagnosis (p = 0.084) and bulky disease at baseline (p = 0.020) appeared to be strong and independent risk factors for TFR.
Risk minimisation measures	Routine risk minimisation measures: • Section 4.2 of SmPC: dose interruption advice for TFR. • Section 4.4 of SmPC warning. • Listed as an ADR in Section 4.8 of SmPC. Additional risk minimisation measures: • Educational HCP brochure.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • RRMCL PASS.

Table 1.2.2-1: Important Identified Risks

Cardiac Failure and Cardiac Arrhythmias	
Evidence for linking the risk to the medicine	Based on clinical trial data, a higher incidence of cardiac failure has been observed. Based on clinical trial data, a higher incidence of cardiac arrhythmias was observed in the lenalidomide arm.
Risk factors and risk groups	No particular risk groups or risk factors have been identified for lenalidomide. In MM and MDS no differences in frequency, severity, serious outcomes and apparent risk level of cardiac failure AEs have been observed. Cardiac symptoms in patients with MDS are often due to anaemia and may be due to iron overload and side effects of therapy. In a study of 840 MDS patients, Della Porta reported that heart failure (28% versus 18%, $p = 0.001$) and cardiac death (69% versus 55%, $p = 0.03$) were significantly more frequent in transfusion-dependent patients. In a Cox analysis with time-dependent covariates, transfusion-dependent patients showed an increased risk of non-leukemic death (HR = 2.12; $p \leq 0.001$), heart failure (HR = 1.34; $p = 0.03$), and cardiac death (HR = 2.99; $p = 0.01$). The development of secondary iron overload significantly affected the risk of non-leukemic death and OS (HR = 1.25 and 1.16, respectively; $p < 0.001$), and this effect was maintained after adjusting for transfusion burden. Iron overload specifically increased the risk of developing heart failure (HR = 1.17, $p < 0.001$). General risk factors for CHF include increasing age, previous heart disease, diabetes, hypertension, amyloidosis, and previous anthracycline based chemotherapy treatment. Standard risk factors for atrial fibrillation include advancing age, European ancestry, body size (greater height and body mass index), electrocardiography features (left ventricular hypertrophy, left atrial enlargement), diabetes, systolic blood pressure and presence of cardiovascular disease (ie, CHD, heart failure, valvular heart disease). Other factors include clinical and subclinical hyperthyroidism, chronic kidney disease, and heavy alcohol consumption. Familial aggregation studies have identified a role for genetic factors, although such factors probably account for a small proportion of cases. In a case-control study of 385 eligible cases of new-onset atrial fibrillation embedded within the Rotterdam study, the risk of new-onset atrial fibrillation was significantly higher for persons who received a corticosteroid prescription within 1 month before the atrial fibrillation index date. Only high-dose corticosteroid use was associated with increased risk (OR = 6.07; 95% CI: 3.90-9.42). The association of atrial fibrillation was independent of indication for use. Risks were increased not only in patients with asthma or chronic obstructive pulmonary disease, but also in patients with rheumatic, allergic, or malignant haematologic diseases.
Risk minimisation measures	Routine risk minimisation measures: • Listed as ADRs in Section 4.8 of SmPC • Listed in PL. Additional risk minimisation measures: • None.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Connect® MM Registry. • Revlimid TNE NDMM Registry. • MDS-012

Table 1.2.2-1: Important Identified Risks

Ischaemic Heart Disease (Including Myocardial Infarction)	
Evidence for linking the risk to the medicine	In clinical trials, ischaemic heart disease has been reported in patients treated with lenalidomide. Myocardial infarction occurs relatively often in individuals of the older age groups that most often develop in the target indications of MM, MDS, MCL and FL.
Risk factors and risk groups	Risk factors for 10-year coronary risk based upon the Framingham Heart Study include elevated blood pressure, elevated cholesterol, high-density lipoprotein-C, presence of diabetes and cigarette smoking. These factors are in addition to the well-known relationships between coronary risk and age and gender. In Europe, smoking remains a major public health issue and about 20% of death from CVD in men and about 3% of deaths from CVD in women are due to smoking. Levels of obesity are high across Europe in both adults and children, although rates vary substantially between countries. Participation in physical activity is low. Increases in population body mass index over the interval 1980 to 2008 were noted in almost all countries. The prevalence of diabetes in Europe is high and has increased rapidly over the last ten years, increasing by more than 50% in many countries.
Risk minimisation measures	Routine risk minimisation measures: • Myocardial infarction is included in Sections 4.4 and 4.8 of the SmPC. Additional risk minimisation measures: • None.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Connect® MM Registry. • Revlimid TNE NDMM Registry. • MDS-012

Table 1.2.2-2: Important Potential Risks

Off-label Use	
Evidence for linking the risk to the medicine	There is potential for the use of lenalidomide in indications other than the approved indications.
Risk factors and risk groups	Not applicable
Risk minimisation measures	Routine risk minimisation measures: • Collection of off-label use data detailed in Section 4.4 of SmPC. Additional risk minimisation measures: • None.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • MDS-012

1.2.3 Post-authorisation Development Plan

1.2.3.1 Studies Which are Conditions of the Marketing Authorisation

The following studies are conditions of the marketing authorisation:

Monitoring of Pregnancy Prevention Programme Implementation

Purpose of the study: Monitoring implementation of the Pregnancy Prevention Programme.

Revlimid TNE NDMM Registry (CC-5013-MM-034)

Purpose of the study: The primary objectives are to compare the incidence of cardiovascular events between TNE NDMM patients treated with a first line lenalidomide-containing regimen and those treated with a first line non lenalidomide-containing regimen; and to identify, quantify, and characterise risk factors for cardiovascular events in this population of TNE NDMM patients.

MDS PASS (MDS-012):

Purpose of the study: The primary objective is to describe the pattern of use of lenalidomide in the clinical routine practice of MDS patients.

1.2.3.2 Other Studies in Post-authorisation Development Plan

Connect® MM: The Multiple Myeloma Disease Registry

Purpose of the study: The primary objectives of the registry are to describe practice patterns of common first-line and subsequent treatment regimens (including lenalidomide-based) in patients with previously untreated MM, whether or not eligible for transplant, as well as diagnostic patterns and occurrence of SPM in a 'real world' population.

Connect® MDS/AML Disease Registry

Purpose of the study: The primary objectives of the registry are to describe patterns for diagnosis, prognosis, treatment, clinical monitoring and outcome measures in patients with MDS, ICUS and AML; to compare routine clinical practice patterns with existing management guidelines (eg, National Comprehensive Cancer Network); to describe treatment patterns and outcomes in del(5q) patients with or without additional cytogenetic abnormalities; and in non-del(5q) patients; and to summarise patient-reported outcomes (eg, health related Quality of Life [HRQoL]) and economic outcomes, and their association with patient characteristics, treatment regimens, and clinical outcomes. Exploratory objectives are to evaluate molecular and/or cellular markers in the blood/bone marrow tissues and oral epithelial cells that may provide further prognostic classification of MDS and AML subtypes and/or may provide information on drug mechanism of action and on-therapy markers predictive of clinical outcomes and potentially impact clinical outcomes with therapy; to summarise the clinical status (eg, overall survival [OS], progression-free survival [PFS], response rate) of patients with or without mutations by treatment regimen, and to analyse the correlation between mutation detection/allele burden in bone marrow and peripheral blood samples. Data regarding SPM are also being collected.

RRMCL PASS (CC-5013-MCL-005)

Purpose of the study: To quantify and characterise the event of tumour flare reaction (TFR) by tumour burden and the proportion of early deaths by tumour burden in patients treated with lenalidomide in a 'real world' setting.