Public Title	Randomized Study of ON 01910.Na in Refractory MDS With Excess Blasts
Scientific Title	Phase III MultiCenter Randomized Controlled Study to Assess Efficacy and Safety of ON 01910.Na 72-Hr Continuous IV Infusion in MDS Patients With Excess Blasts Relapsing After or Refractory to or Intolerant to Azacitidine or Decitabine
Short Title	ONO 1910
Id KN/ELN	LN_NN_2010_473
Trialgoup	NN
Type of Trial	multicentric, randomized, open-label
Phase	Phase III
Disease	Myelodysplastic Syndrome(MDS) Intermedia II and high risk
Stage of Disease	.
Aim	- Overall survival - Overall response (complete and partial remission) according to 2006 IWG criteria - Complete bone marrow response according to 2006 IWG criteria - Hematological improvements according to 2006 IWG criteria - Scores of Quality of Life Questionnaire - Adverse events - Change in Aneuploidy - Transition time to AML - Incidence of infections and bleeding episodes.
Inclusion Criteria	- MDS diagnosis confirmed within 6 weeks prior to entry according to WHO or FAB classification - MDS classified as follows, according to WHO and FAB classification: - a. RAEB-1 (5% - 9% BM blasts) - b. RAEB-2 (10% - 20% BM blasts) - c. CMML (10% - 20% BM blasts) and WBC < 13,000/L - d. RAEB-t (21% - 30% BM blasts), with following criteria: - aa. WBC < 25 x 10E9/L at entry - bb. Stable WBC at least 4 weeks prior to entry and not requiring intervention for WBC control with hydroxyurea, chemotherapy, or leukopheresis. - At least one cytopenia (ANC < 1800/µL or platelet count < 100,000/µL or hemoglobin <10 g/dL) - Progression according to 2006 International Working Group (IWG) criteria any time after start of azacitidine or decitabine during past 2 years; or failure to achieve complete or partial response or hematological improvement (according to 2006 IWG) after at least six 4-week cycles of azacitidine or four 6-week cycles of decitabine during past 2 years; or relapse after initial complete or partial response or hematological improvement (according to 2006 IWG criteria) observed after at least six 4-week cycles of azacitidine or four 6-week cycles of decitabine during past 2 years; or, intolerance to azacitidine or decitabine defined by drug-related Grade 3 liver or renal toxicity leading to discontinuation during the past 2 years. - Did not respond to, relapsed after, not eligible for, or opted not to do bone marrow transplantation - Off other MDS treatments for at least 4 weeks; Filgrastim (G-CSF) and erythropoietin allowed before and during the study as clinically indicated. - No need for induction chemotherapy - ECOG status 0, 1 or 2

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- Willing to adhere to protocol prohibitions and restrictions
- Patient (or a legally authorized representative) must sign informed consent form to indicate patient's understanding study's purpose and procedures and willingness to participate

Exclusion Criteria

- Anemia due to factors other than MDS (including hemolysis or gastrointestinal bleeding) unless stabilized for 1 week after RBC transfusion.
- Any active malignancy within the past year, except basal cell or squamous cell skin cancer or carcinoma in situ of the cervix or breast
- Uncontrolled intercurrent illness including, but not limited to, symptomatic congestive heart failure, unstable angina pectoris, or cardiac arrhythmia
- Active infection not adequately responding to appropriate therapy
- Total bilirubin >=1.5 mg/dL not related to hemolysis or Gilbert's disease.
- Alanine transaminase (ALT)/aspartate transaminase (AST) >= 2.5 x upper limit of normal (ULN)
- Serum creatinine >= 2.0 mg/dL
- Ascites requiring active medical management including paracentesis, or hyponatremia (defined as serum sodium value of <130 mEq/L)
- Pregnant or lactating females
- Patients unwilling to follow strict contraception requirements (including condom use for males with sexual partners, and for females: prescription oral contraceptives [birth control pills], contraceptive injections, intrauterine device, double-barrier method [spermicidal jelly or foam with condoms or diaphragm], contraceptive patch, or surgical sterilization) before entry and throughout the study
- Females with reproductive potential who do not have a negative urine beta-human chorionic gonadotropin pregnancy test at screening
- Major surgery without full recovery or major surgery within 3 weeks of ON 01910.Na treatment start
- Uncontrolled hypertension (defined as systolic pressure 160 mmHg and/or diastolic pressure 110 mmHg)
- New onset seizures (within 3 months prior to first dose of ON 01910.Na) or poorly controlled seizures
- Any other concurrent investigational agent or chemotherapy, radiotherapy, or immunotherapy
- Prior treatment with low-dose cytarabine during past 2 years Investigational therapy within 4 weeks of starting ON 01910.Na
- Psychiatric illness or social situation that limits the patient's ability to tolerate and/or comply with study requirements

Age >= 18 years

Status No longer recruiting

start of Recruitment 01.11.2010

Target Sample Size 270

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