DS2325-119

Titre de l'essai

« Une étude visant à explorer l'innocuité, la pharmacocinétique et le signal clinique précoce d'efficacité du DS-2325a chez les patients atteints du syndrome de Netherton»

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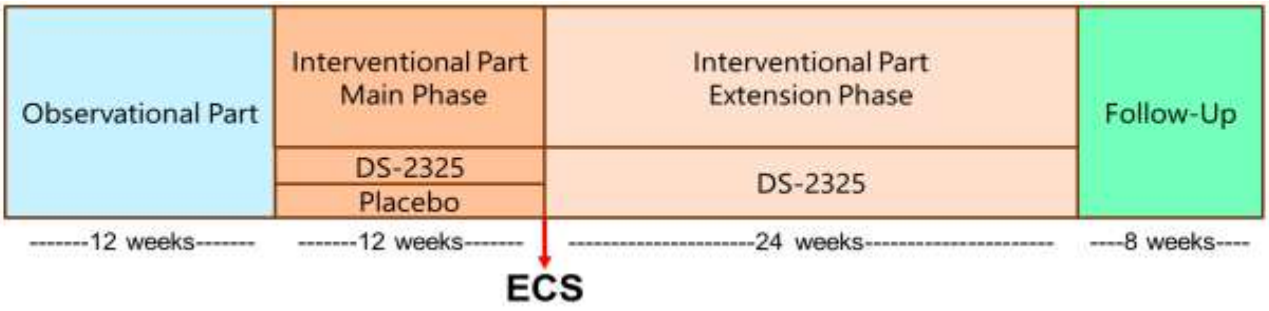
https: https://clinicaltrials.gov/ct2/show/NCT05979831

Population cible :
Cette étude explorera l'innocuité, la pharmacocinétique (PK) et l'efficacité du signal clinique précoce du DS-2325a chez les patients adultes atteints de NS. L'objectif principal de l'étude sera d'explorer l'innocuité et la tolérabilité du DS-2325a chez les patients atteints de NS en administrant du DS-2325a chaque semaine pendant 12 semaines consécutives (phase principale, qui sera en double aveugle et au cours de laquelle certains participants recevront placebo comme contrôle) et de confirmer en administrant pendant 24 semaines supplémentaires (phase d'extension, qui sera ouverte et pendant laquelle tous les participants recevront DS-2325a). Les objectifs secondaires de l'étude comprendront l'exploration des propriétés pharmacocinétiques, de l'efficacité et de l'immunogénicité du DS-2325a chez les patients atteints de NS en administrant du DS-2325a chaque semaine pendant 12 semaines consécutives (phase principale) et de confirmer en administrant pendant 24 semaines supplémentaires (phase de prolongation

Traitement à l'étude : DS-2325a

Schéma de traitement :



L'étude se compose de 5 parties :
- Sélection (4 semaines au maximum)
- Observationnelle (12 semaines)
- Interventionnelle – Phase principale (12 semaines)
- Interventionnelle – Phase d'extension (24 semaines)
- Suivi (8 semaines)

Rythme des visites :

16.3. Schedule of Events

Table 3 Visit Schedule for Observational Part and Interventional Part-Main Phase

Schedule of Events		Observational Part			Interventional Part-Main Phase											
	Screening*				Baseline^											
Week	−4 to 0	1	5	9	1	2	3	4	5	6	7	8	9	10	11	12
Visit Window allowed (day)		±1	±1	±1	±1	±1	±1	±1	±1	±1	±1	±1	±1	±1	±1	±1

Table 4 Visit Schedule for Interventional Part-Extension Phase

Schedule of Events	Interventional Part-Extension Phase																								Follow-Up	
																									EOT	EOS
Weeks	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	45
Visits window allowed (Day)	±1	±1	±1	±1	±1	±1	±1	±1	±1	±1	±1	±1	±1	±1	±1	±1	±1	±1	±1	±1	±1	±1	±1	±1	±1	±3

Critères d'inclusion	O	N
4.1. Inclusion Criteria 4.1.1. Screening Patients must satisfy all of the following criteria to be included in the study: 1. Male or female patients aged 18 to 65 years with clinical diagnosis of NS including at least 3 out of the 4 following clinical criteria: □ Neonatal erythroderma, □ Bamboo hair and/or alopecia, □ Chronic atopy specified as food allergy and/or asthma and/or rhino-conjunctivitis and/or eczema for at least 2 years, □ Ichthyosis linearis circumflexa or scaling erythroderma or equivalent. 2. Immunohistochemistry documentation of absence of LEKTI in the skin or confirmed SPINK5 gene mutations. 3. NS involvement of ≥20% of Body Surface Area (BSA). 4. Patients must give written informed consent to participation in the study prior to Screening. 5. Patients must be willing and able to understand and comply with study requirements. 6. Patients must be willing to have skin tape harvests collected from lesional and nonlesional skin areas. 7. All women must have a negative serum pregnancy test at Screening. Women must not be lactating. 8. Women of childbearing potential (not post-menopausal as a result of either natural or post-surgery cessation of menses) with male partner must be willing to practice effective contraception during the study, starting at Screening and continuing for 3 months after the last dose of study drug. Methods of highly effective contraception include 1) hormonal administration of estrogen and progestogen combined, which may be given in oral, intravaginal or transdermal form or of progestogen only, which may be given in oral, injectable or implantable form; 2) use of intrauterine devices, including intrauterine hormone-releasing devices; 3) bilateral tubal occlusion; 4) vasectomy of partner; and 5) complete sexual abstinence. 4.1.2. Baseline (Main Phase-Interventional Part) At Week 1 Baseline Visit, patients must continue to satisfy all of the following criteria before continuing to the Interventional Part of the study: 1. NS involvement of ≥20% of BSA. . All women must have a negative urine pregnancy test at Baseline. Women must not be lactating.		

3. Women of childbearing potential (not post-menopausal as a result of either natural or post-surgery cessation of menses) with male partner must be willing to practice effective contraception during the study, starting at Screening and continuing for 3 months after the last dose of study drug (refer to Section 4.1.1 for methods of highly effective contraception). 4. Patients must agree not to participate in any other investigational study during study drug administration and for 3 months after the last dose of study drug.		

Critères d'exclusion	O	N
4.2. Exclusion Criteria 4.2.1. Screening Patients who meet any of the following criteria will be disqualified from entering the study: 1. Any skin disease that may interfere with the diagnosis or evaluation of NS. 2. Cutaneous infection requiring treatment with systemic antibiotics, antivirals, antiparasitics, or antifungals within 2 weeks before Screening visit. 3. Concomitant systemic disease not controlled by treatment. Stability for 3 months prior to Screening is required. 4. Kidney or liver disease with significant impairment of organ function (creatinine clearance <30 mL/min, calculated using the Cockcroft-Gault Equation, and Child-Pugh Class C). 5. Concomitant disease or condition that may interfere with, or treatment of which may interfere with, the conduct of the study or that would, in the opinion of the Investigator, pose an unacceptable risk to the patient in this study. 6. Any significant condition (eg, medical, psychiatric, or social) that according to Investigator’s judgment would prevent compliance with study protocol and full study participation.		

7. Known hypersensitivity to any ingredient of the study drug product. 8. Anticipation of the need for surgery or hospitalization during the study. 9. History of suicide attempt or suicidal ideation within 1 year prior to Screening. 10. History of substance abuse within 6 months prior to Screening or a positive urine drug test at Screening. Medical marijuana may be used per discretion of the Investigator. 11. History or positive test result for human immunodeficiency virus (HIV) at Screening. 12. Active hepatitis B virus (HBV) infection, determined by positive test result for hepatitis B surface antigen, at Screening. 13. Active hepatitis C virus (HCV) infection, determined as HCV ribonucleic acid (RNA) 4. Use of topical drugs that may alter the course of NS (eg, topical corticosteroids and topical calcineurin inhibitors) within 2 weeks before Screening or anticipation of need to use these drugs during study drug. 15. Systemic treatment with corticosteroids, immunosuppressants, targeted therapeutics, biologics, and IV Ig within 8 weeks before Screening. 16. Participation in any other clinical study or expanded access program with an investigational drug or device within 4 weeks before Screening. 17. Suspected or confirmed COVID-19 within 4 weeks before or ongoing at Screening and planned vaccination against COVID-19 during study drug. 4.2.2. Baseline (Main Phase-Interventional Part) At Week 1 Baseline Visit, patients must continue to not meet any of the following criteria before continuing to the Interventional Part of the study: 1. Cutaneous infection requiring treatment with systemic antibiotics, antivirals, antiparasitics, or antifungals within 2 weeks before Baseline visit. 2. Concomitant disease or condition that may interfere with, or treatment of which may interfere with, the conduct of the study or that would, in the opinion of the Investigator, pose an unacceptable risk to the patient in this study. 3. Any significant condition (eg, medical, psychiatric, or social) that according to Investigator's judgment would prevent compliance with study protocol and full study participation. 4. Anticipation of the need for surgery or hospitalization during the study. 5. Use of topical drugs that may alter the course of NS (eg, topical corticosteroids and topical calcineurin inhibitors) within 2 weeks before Baseline or anticipation of need to use these drugs during study drug. 6. Systemic treatment with corticosteroids, immunosuppressants, targeted therapeutics, biologics, and IV Ig within 8 weeks before Baseline. 7. Participation in any other clinical study or expanded access program with an investigational drug or device within 4 weeks before Baseline. 8. Suspected or confirmed COVID-19 within 4 weeks before or ongoing at Baseline and planned vaccination against COVID-19 during study drug.		