

Effects of probiotic supplementation in adult with atopic dermatitis: a systematic review with meta-analysis

Running head: Probiotics in adult atopic dermatitis

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What is already known about this topic?

- Analyses about the effect of probiotic administration on the severity of adult atopic dermatitis (AD) show inconsistent results as of yet.

What does this study add?

- Our meta-analysis supports a role of certain probiotics as a therapeutic tool for the treatment of adult AD, particularly in severe cases.
- Efficacy of probiotics is strain-specific, and *L. salivarius* and *L. acidophilus* confer the largest clinical benefit.
- Such benefit is apparently independent of IgE levels and eosinophil count.
- Despite of these encouraging results, decrease in AD severity did not seem to translate into a better quality of life, as assessed by the Dermatology Life Quality Index (DLQI).

Abstract

Background: Atopic dermatitis (AD) is one of the most common chronic inflammatory skin disease. The effect of probiotic administration on the severity of adult patients with AD have shown inconsistent results. We aimed to determine the effectiveness of probiotic supplementation as a therapeutic tool for adult AD.

Methods: PubMed, Scopus, and EMBASE were systematically queried to collect data from studies in which probiotics were administered to treat adult AD.

Results: Out of 413 publications, 9 papers were included in the meta-analysis.

Significant differences in SCORAD favoring probiotics were observed (RR:-5.93

95%CI: -8.43 – -3.43). *L. salivarius* presented with the major effect size (RR:-9.79

95%CI: -13.04 – -6.54), followed by *L. acidophilus* (RR:-5.77 95%CI: -10.82 – -0.72)

and *L. plantarum* (RR:-3.76 95%CI: -6.36 – -1.16). No benefit was observed with *L. fermentum*. Based on the severity of AD, probiotics showed better results in subjects with moderate to severe AD (RR:-9.12 95%CI: -12.17 – -6.08) than in individuals with mild disease (RR:-2.67 95%CI: -4.67 – -0.66). Serum levels of IgE and eosinophil count remained significantly unchanged after the probiotic intervention (RR: 0.25 95%CI: -0.10 – 0.60; RR: -0.27 95%CI: -0.68 – 0.13).

Conclusion: Current evidence supports a role of certain probiotics as a therapeutic tool for the treatment of adult AD, particularly in severe cases. The efficacy of probiotics is strain specific, being *L. salivarius* and *L. acidophilus* with the largest clinical benefit. Such benefit is apparently independent of IgE levels and eosinophil count. Despite of these encouraging results, decrease in AD severity did not translate into a better quality of life assessed by DLQI. Current data precluded us to obtain reliable data on the optimal dose and duration of probiotic treatment.

Introduction

Atopic dermatitis (AD) is one of the most frequent and complex chronic inflammatory skin disease with a variety of clinical features depending on age, race and genetic background¹. This disease requires active intervention since it is often accompanied by sleep disturbance, depression, anxiety and food allergies in addition to skin lesions^{2,3}.

Recent advances in understanding skin barrier dysregulation, innate and adaptive immune imbalance, and altered skin microbiomes have shown the development of AD seems closely associated with changes in gut microbial diversity and composition⁴⁻⁶.

Consequently, a growing body of researches has hinted that probiotics may be beneficial in the prevention and treatment of pediatric AD through the modulation of host immune responses⁷⁻⁹. However, whether the “gut-skin” axis can also be cataloged

as a therapeutic option using probiotics in adult AD patients is still a matter of debate and uncertainty, since available data demonstrate inconsistent results^{5,6}. Hence, we conducted a systematic review with meta-analysis to analyze the potential benefit(s) of probiotics to manage adult AD, and ultimately, to help clinicians and patients make evidence-based decisions about this intricate issue.

Material and methods

This review was carried out in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses¹⁰.

1. Data sources:

Two independent investigators (H.H-E and M.S.) systematically identified studies in the Pubmed, Embase and Scopus databases (from inception through March 10th 2022) for all potentially relevant articles regarding the potential therapeutic effect of probiotic supplementation on adult AD patients. We applied the following medical subjects heading (MeSH) terms: “probiotics” AND “atopic dermatitis” OR “atopic eczema” OR “atopy”. Additionally, we also examined the reference list of each selected paper for further relevant articles.

2. Inclusion criteria

Articles had to meet the following criteria to be included in our meta-analysis: (1) studies must be randomized controlled trials or prospective studies with a placebo group, (2) participants enrolled must be adults (> 18 years) diagnosed with AD previously, (3) reports must assess the clinical effect with the SCORing AD (SCORAD)

index. (4) studies or their abstract must be published in English. All records failing to meet these criteria were excluded.

3. Data extraction, assessment of quality and statistical management

The main endpoint was the SCORAD score after the intervention with probiotics. Other secondary outcomes included: the impact in quality of life assessed by the Dermatology Life Quality Index (DLQI), changes in the serum levels of IgE and eosinophils count. The quality of the included trials was assessed with the three parameters of the Jadad scale: randomization, double blinding and reported dropouts¹¹. The statistical management of the data was conducted as previously reported by the authors¹².

Results

As shown in Figure 1, the systematic literature search retrieved 426 potentially relevant articles and 413 papers were excluded after screening the titles, while thirteen papers were selected for full reading. After full reading of these remaining articles, three records assessing the clinical effect with other score apart from SCORAD¹³⁻¹⁵ and one record comprising healthy subjects as controls¹⁶ were excluded. Finally, 9 papers comprising 400 individuals (217 receiving probiotics and 183 receiving placebo) met the inclusion criteria and were selected for meta-analysis¹⁷⁻²⁵. Table 1 depicts the characteristics of these studies with their Jadad score.

SCORAD

The probiotic intervention reduced the severity of adult AD patients measured by SCORAD compared to placebo (RR:-5.93 95%CI: -8.43 – -3.43, I²=96%). In the subgroup analysis by probiotic strains, *Lactobacillus salivarius* presented with the

major effect size (RR:-9.79 95%CI: -13.04 – -6.54, $I^2=97\%$, three studies), followed by *Lactobacillus acidophilus* (RR:-5.77 95%CI: -10.82 – -0.72, $I^2=0\%$, two studies) and *Lactobacillus plantarum* (RR:-3.76 95%CI: -6.36 – -1.16, $I^2=0\%$, two studies). No benefit was observed with *Lactobacillus fermentum*. The forest plot of these findings is represented in Figure 2. As shown in Figure 3, the subgroup analysis by baseline severity of AD showed probiotics were effective in treating subjects with moderate to severe AD (RR:-9.12 95%CI: -12.17 – -6.08, $I^2=95\%$, four studies), and also in individuals with mild disease, though the benefit was lower (RR:-2.67 95%CI: -4.67 – -0.66, $I^2=62\%$, five studies).

DLQI

Three trials investigated the effect of probiotics in the quality of life, and the meta-analysis estimated that this intervention did significantly improve the DLQI index (RR:-1.15 95%CI: -1.91 – -0.39, $I^2=75\%$). Figure 4 depicts the forest plot of the DLQI analysis.

Serum IgE and eosinophil count

The serum levels of IgE remained significantly unchanged after the probiotic intervention versus placebo (RR: 0.25 95%CI: -0.10 – 0.60, $I^2=0\%$, three studies. Figure 5A). Equally, the use of probiotic did not demonstrate an effect on the eosinophil count (RR: -0.27 95%CI: -0.68 – 0.13, $I^2=85\%$, two studies. Figure 5B).

Discussion

In our meta-analysis, we have observed the probiotic supplementation can decrease the severity of AD, as measured by SCORAD. Notably, the effect of probiotics in adult AD

has not been investigated the current literature as thoroughly as for the pediatric population: the evidence of probiotic in children with AD is largely supported by several meta-analyses^{9,26-29}, while in adult AD, to our best knowledge, only two meta-analyses have addressed this question as of yet. The first of these two works included 4 trials involving 120 participants³⁰, whilst the second study comprised 6 trials involving 241 patients³¹. Certain articles contained in these former meta-analyses were excluded in our work due to the appraisal of size effect different than SCORAD (i.e. Skindex-29-J¹³, grading system of AD severity by Rajka and Langelland¹⁴, classification of AD severity by the Japanese Dermatological Association¹⁵) and the application of healthy subjects as controls instead of AD patients¹⁶. Even with these exclusions intended to reduce the heterogeneity among trials, our study involved 9 papers with 400 subjects, thus comprising the largest meta-analysis on this topic so far.

According to our results, use of probiotics can lead to a mean reduction in SCORAD of 5.93. Previous studies yielded larger mean SCORAD reductions of 8.26 and 7.90^{30,31}, but since their methodology incorporated a higher heterogeneity with a substantially lesser number of participants in the analysis, it is feasible to expect our result is closer to the real effect of probiotics on the modulation of AD severity.

In the pediatric AD population, a recent meta-analysis has shown that use of probiotics decreased SCORAD by 3.13 points on average⁹. Other previous meta-analyses in this population have reported similar levels of reduction in SCORAD (3.04, 4.50, 5.74 and 6.11 respectively)²⁶⁻²⁹. Based on our findings, it is rational to state that the recent encouraging results of probiotics in infant AD can be extrapolated to certain extent also to adult AD individuals, particularly in moderate to severe cases, in whom probiotics induced up a decrease in the SCORAD value up to 4-fold compared to mild cases.

Probiotics have demonstrated an immunomodulatory effect in the adaptive and innate immune systems and an ability to reduce the inflammatory response in AD, which subsequently has an impact on pruritus and skin barrier function³². In this context, our meta-analysis revealed that the potential antiinflammatory effect of probiotics appears to be independent of IgE levels and eosinophil count as there was no difference in these outcomes between the probiotic group and the placebo group. Other mechanisms such as the TARC/CCL17, which was recently shown to be an early marker for AD in children³³ or the toll-like receptor (TLR) signalling, particularly TLR-9, may be involved with the outcome of AD under probiotic therapy in adults³⁴. However, considering the small number of subjects analyzed, our finding should be interpreted with caution.

A key finding, not previously reported, of our subgroup analysis is that the beneficial effect of probiotics was dependant on strain type; indeed some specific strains such as *L. salivarius* and *L. acidophilus* proved to be more effective than others in decreasing the SCORAD. The meta-analysis conducted by Kim et al³⁰ lacked a subgroup analysis by specific strains as in our study. The authors conducted a subanalysis by genera and they concluded that the *Lactobacillus* species have a larger effect than *Bifidobacterium* species. Notably, in infant individuals with AD, the strains showing the largest decrease in SCORAD were *L. paracasei* and *L. sakei*⁹. This suggests that the optimal strains to treat AD patients differs depending on the age of patients: Probably, a sort of specificity for probiotics exists according to the stage of life (infant, adolescence and adulthood) as a reflection of the distinctive composition of gut microbiota developed throughout the normal colonization of the human gut³⁵. The novelty of our finding holds important clinical implications since the supplementation with a precise mixture of the most

relevant strains might improve the clinical outcomes of probiotic treatment in adult AD patients. Hence, this question warrants to be investigated in future prospective trials.

Analysis of the data also showed a statistically significant difference in the quality of life of AD patients with the probiotic supplementation leading to a mean DLQI reduction of -1.15. Another previous meta-analysis obtained a similar average decrease of -0.96³¹. Since the minimal clinically important difference of the DLQI score in inflammatory skin diseases has been established in 4³⁶, the real impact of probiotics on the quality of life of AD patients is allegedly irrelevant or it needs additional large scale studies with optimized composition of the probiotics.

Some limitations have to be acknowledged: First, the investigation of dose by a subgroup analysis was unfeasible because of the high heterogeneity among the included studies that tested diverse doses with various probiotic strains. Second, we did not find any changes in AD severity regarding the duration of treatment (<8 weeks versus ≥ 8 weeks; data not shown). Thus, future trials with standardized doses and durations of probiotics are required to set up the optimal dose and duration of probiotic treatment.

Conclusion

Current evidence supports a role of probiotics as a therapeutic tool for the treatment of adult AD, particularly in severe cases. The efficacy of probiotics is strain-specific, and *L. salivarius* and *L. acidophilus* confer the largest clinical benefit. Such benefit is apparently independent of IgE levels and eosinophil count and hence, other mechanisms of action targeting the proinflammatory response may be implicated. Despite of these encouraging results, the decrease in AD severity does not seem to translate into a better quality of life assessed by DLQI, which may be due to the inadequate composition of strains and time points chosen. Larger scale, double blinded prospective

studies are demanded to clarify as to whether probiotics do not only reduce skin lesions, but also improve quality of life of AD patients measured by DLQI or other tools such the patient-oriented eczema measure (POEM). Along that line, future studies should also include as to whether probiotics may be capable of reducing the itch score in patients. Current data precluded us to obtain reliable data on the optimal dose and duration of probiotic treatment. These unmet questions should be addressed in future studies.

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Figure legends

Figure 1. PRISMA diagram of the literature search.

Figure 2. Forest plot showing the difference in SCORAD for probiotics in the treatment of atopic dermatitis stratified by strain.

Figure 3. Forest plot showing the sub-meta-analysis stratified by disease severity.

Probiotics were effective in treating subjects with moderate to severe atopic dermatitis, and also in individuals with mild disease, though the benefit was lower.

Figure 4. Forest plot of the impact of probiotic supplementation in the quality of life measured by the Dermatology Life Quality Index (DLQI).

Figure 5. Forest plot of impact of probiotic supplementation in the IgE levels (5A) and in the eosinophil counts (5B). Both outcomes did not differ between the probiotic and the placebo groups.

1

2 Table 1. Characteristics of studies included in the meta-analysis. * DB: double blinded.

3 PPT: prospective pilot trial. RCT: Randomized controlled trial. SB: single blinded.

REFERENCE (LOCATION)	METHOD *	N (Intervention / Control)	INTERVENTION (DOSE)	TIME OF EXPOSURE	SEVERITY OF AD	JADA SCALE Randomisation/ Blinding/Withdrawals (total)
- Drago, 2011 (Italy)	DB, RCT	19/19	<i>L. salivarius</i> (1 x10 ⁹ twice daily)	16 weeks	Moderate to severe	1+1/1+1/1 (5)
- Drago, 2014 (Italy)	SB, RCT	13/12	<i>L. salivarius</i> (5 x10 ⁹ twice daily)	4 weeks	Moderate	1 / 0 / 1 (2)
- Fang, 2020 (China)	SB, RCT	41/25	<i>L. plantarum</i> (1 x10 ⁹ daily)	8 weeks	Mild to moderate	1 / 0 / 1 (2)
- Iemoli, 2012 (Italy)	DB, RCT	31/15	<i>L. salivarius</i> + <i>B. breve</i> (1 x10 ⁹ twice daily)	12 weeks	Moderate	1 / 1+1/ 1 (4)
- Inoue, 2014 (Japan)	DB, RCT	24/25	<i>L. acidophilus</i> (20.7 mg/day)	8 weeks	Moderate to severe	1 / 1+1/ 0 (3)
- Kaur, 2008 (Estonia)	SB, PPT	10/6	<i>L. fermentum</i> (3 x10 ⁹ daily)	12 weeks	Mild	1 / 0 / 0 (1)
- Michelotti, 2021 (Italy)	DB, RCT	40/40	<i>L. plantarum</i> (1 x10 ⁹ daily) + <i>L.</i> <i>reuteri</i>	8 weeks	Mild	1+1 / 1+1 / 1

			(1 x10 ⁹ daily) + <i>L. rhamnosus</i> (1 x10 ⁹ daily)			(5)
- Prakoeswa, 2020 (Indonesia)	DB, RCT	15/15	<i>Lactobacillus plantarum</i> (2 x10 ¹⁰ daily)	8 weeks	Mild to moderate	1+1 / 1+1 / 1 (5)
- Yamamoto, 2016 (Japan)	DB, RCT	24/26	<i>L. acidophilus</i> (20.7 mg/day)	24 weeks	Mild to moderate	1+1 / 1+1 / 1 (5)

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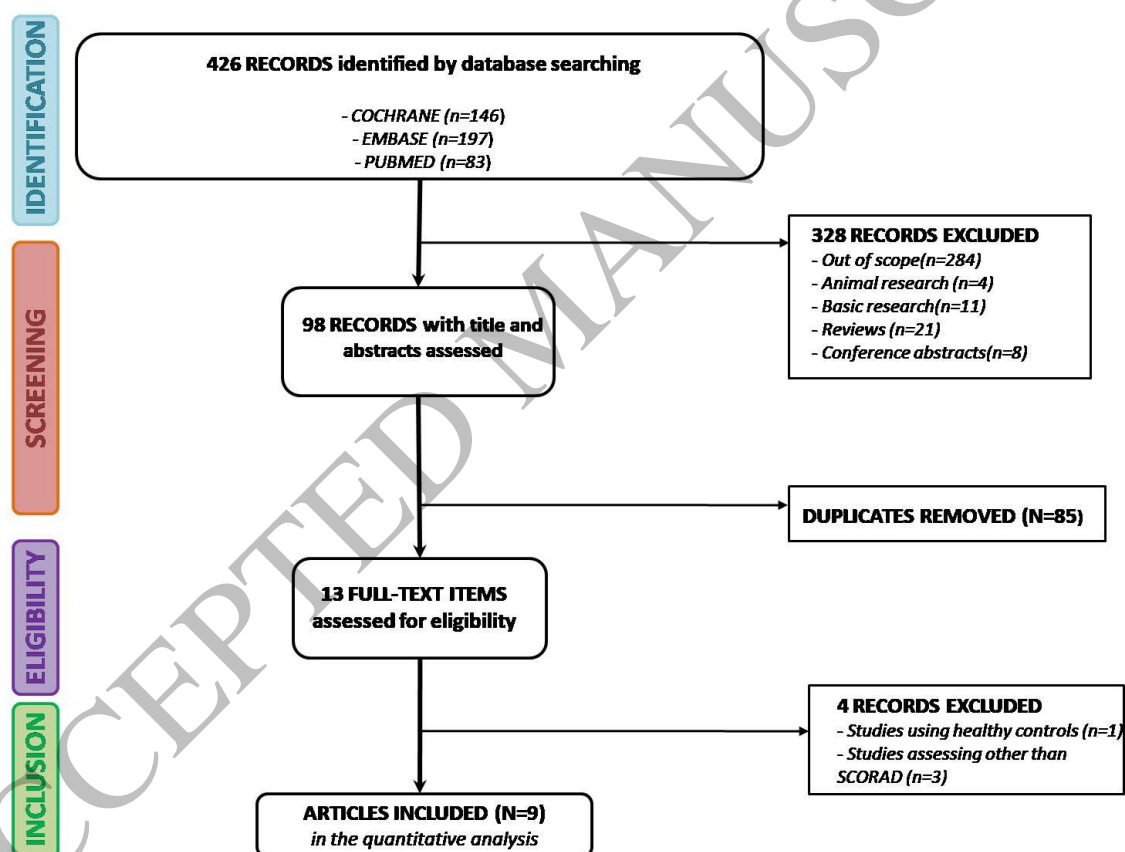


Figure 1
150x117 mm (x DPI)

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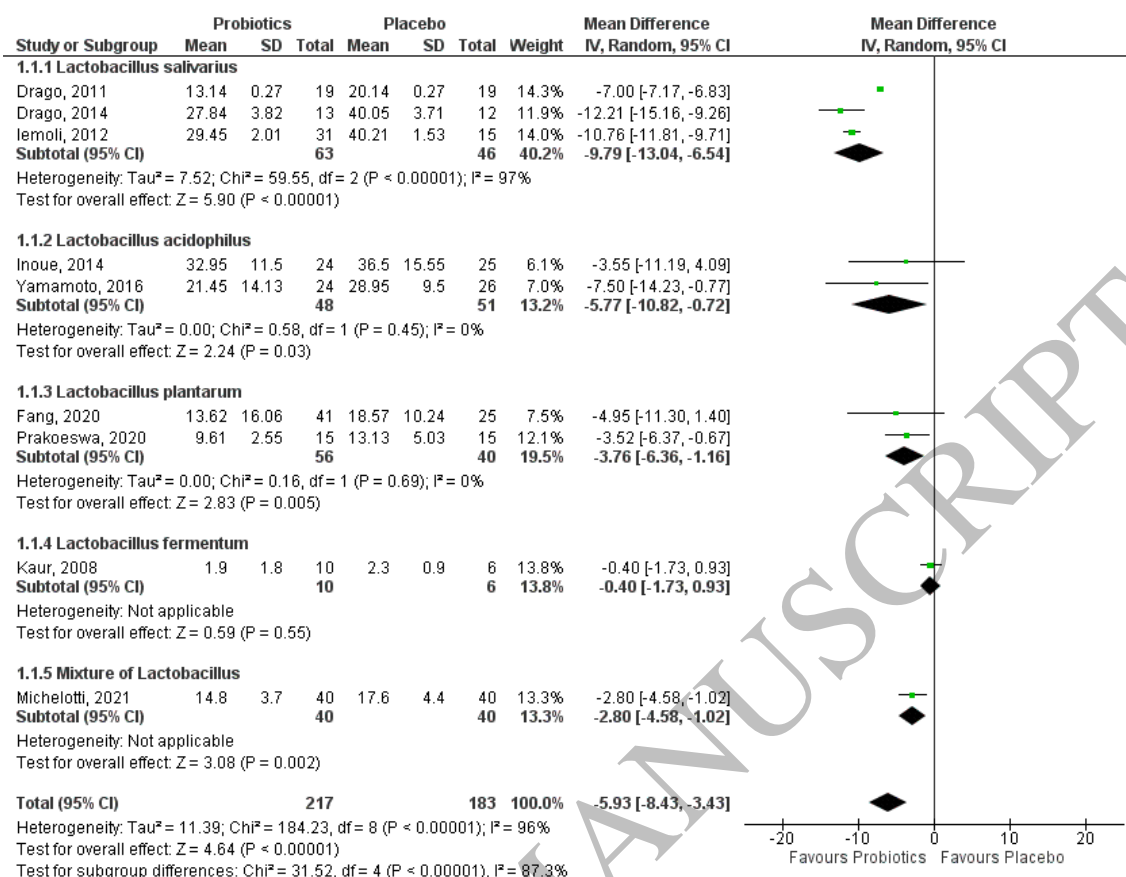


Figure 2
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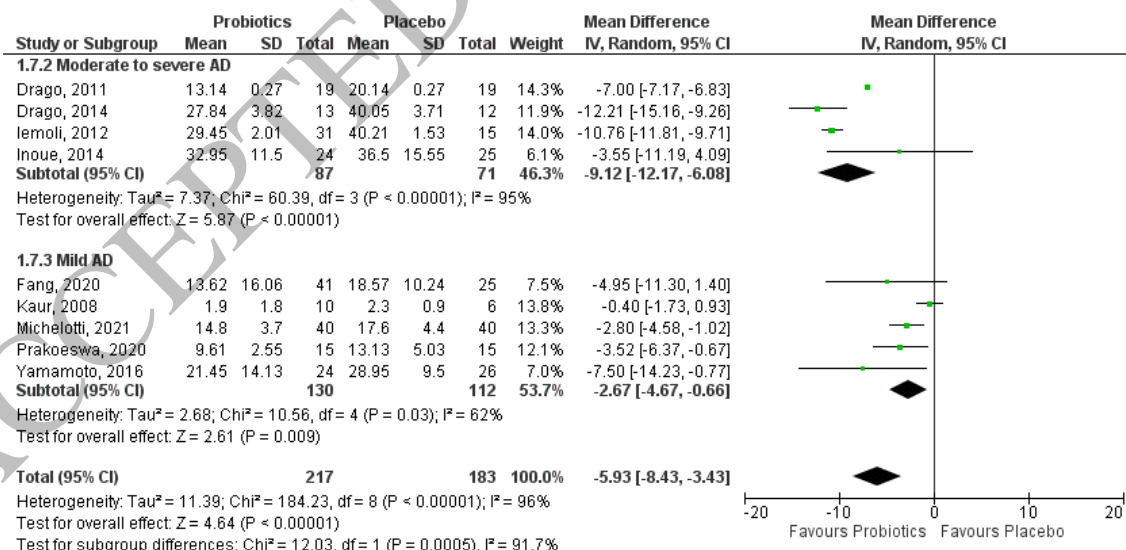


Figure 3
150x72 mm (x DPI)

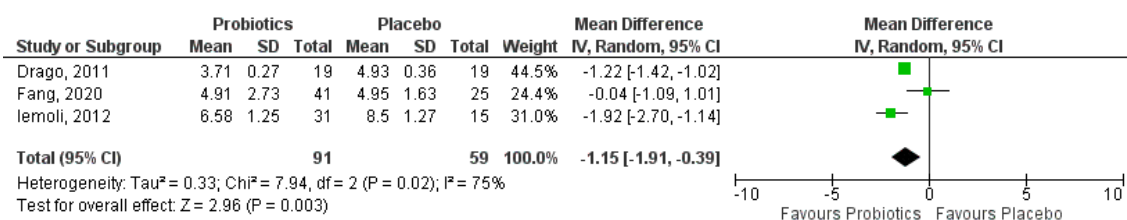


Figure 4
150x29 mm (x DPI)

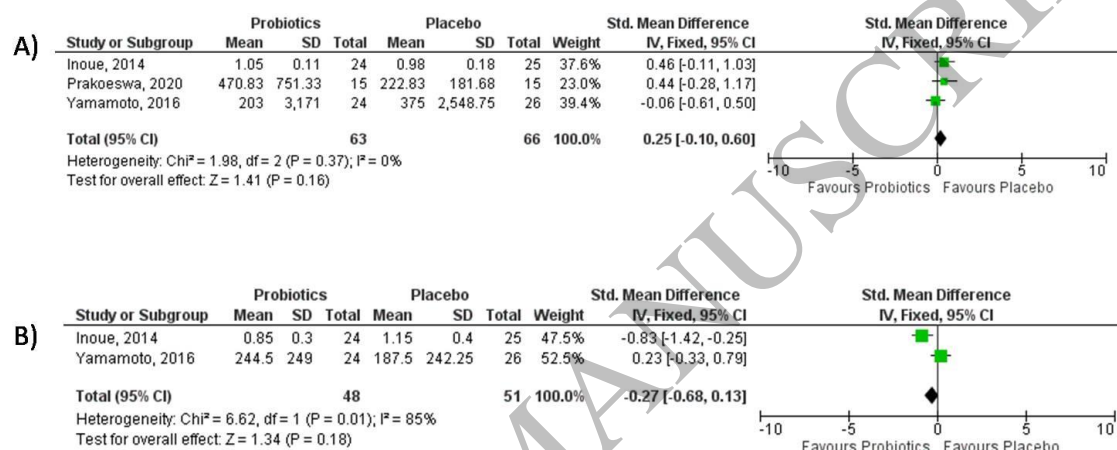


Figure 5
150x60 mm (x DPI)

CHANGING THE LANDSCAPE OF ORAL PSORIASIS TREATMENT¹⁻⁴

SOTYKTU is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy¹



SOTYKTU is a novel, efficacious oral treatment that is generally well-tolerated^{1-4*}



DURABLE EFFICACY

Demonstrated superior PASI 75 response rates, and rates of clear or almost clear skin (sPGA 0/1), vs. placebo at Week 16 (co-primary endpoints)^{2,3*}

PASI 75 response rates were observed at Week 24 and maintained at Week 52^{1*}



GENERALLY WELL-TOLERATED

The most commonly reported adverse reaction is upper respiratory infections (18.9%)¹

Less than 3% of patients discontinued treatment due to AEs between Weeks 0–16¹⁻⁴



ONCE DAILY, ORAL DOSING

Once-daily, oral treatment that can be taken with or without food, with no routine blood monitoring requirements after initiation and no identified DDIs^{1†}



Learn more at
sotyktu.co.uk



Adverse events should be reported. Reporting forms and information can be found at: UK – via the yellow card scheme at: www.mhra.gov.uk/yellowcard, or search for MHRA Yellow Card in the Google Play or Apple App Store. Ireland – via HPRA Pharmacovigilance at www.hpra.ie. Adverse events should also be reported to Bristol-Myers Squibb via medical.information@bms.com or 0800 731 1736 (UK); 1 800 749 749 (Ireland)

*SOTYKTU was studied in two global, Phase 3, randomised, multi-arm clinical studies: POETYK PSO-1 and PSO-2. **PASI 75 and sPGA 0/1 vs. placebo at Week 16 were co-primary endpoints.**

PASI 75 was defined as $\geq 75\%$ reduction from baseline in the Psoriasis Area and Severity Index. sPGA was defined as sPGA score of 0 or 1 with ≥ 2 -point improvement from baseline. N numbers: PSO-1: SOTYKTU (n=332); apremilast (n=168), placebo (n=166); PSO-2: SOTYKTU (n=511); apremilast (n=254), placebo (n=255). SOTYKTU delivered superior PASI 75 response rates vs placebo (PSO-1: 58.4% vs. 12.7%, $p < 0.0001$; PSO-2: 53.0% vs. 9.4%, $p < 0.0001$) at Week 16, and superior results achieving clear or almost clear skin (sPGA 0/1) vs. placebo (PSO-1: 53.6% vs. 7.2%, $p < 0.0001$; PSO-2: 49.5% vs. 8.6%, $p < 0.0001$) at Week 16 (co-primary endpoints).^{2,3}

[†]Via enzyme inhibition, enzyme induction, or transporter inhibition.¹

Abbreviations: AE, adverse event; DDI, drug-drug interaction; PASI, Psoriasis Area and Severity Index; sPGA, static Physician's Global Assessment; TYK2, tyrosine kinase 2.

References:

1. SOTYKTU. Summary of Product Characteristics.

2. Armstrong A *et al.* *J Am Acad Dermatol.* 2023;88(1):29–39.

3. Strober B *et al.* *J Am Acad Dermatol.* 2023;88(1):40–51.

4. SOTYKTU. European Product Assessment Report (EPAR). 26 January 2023. Available at https://www.ema.europa.eu/en/documents/assessment-report/sotyktu-epar-public-assessment-report_en.pdf (Accessed September 2023).

SOTYKTU▼ (deucravacitinib) PRESCRIBING INFORMATION

Great Britain

Consult Summary of Product Characteristics (SmPC) before prescribing. **This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information.**

PRESENTATION: Film-coated tablet containing 6 mg of deucravacitinib.

INDICATION: Treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.

DOSAGE AND ADMINISTRATION: Treatment should be initiated under the guidance and supervision of a physician experienced in the diagnosis and treatment of psoriasis. Posology: 6 mg orally once daily. If a patient shows no evidence of therapeutic benefit after 24 weeks, treatment discontinuation should be considered. The patient's response to treatment should be evaluated on a regular basis. Special populations: *Elderly:* No dose adjustment is required in elderly patients aged 65 years and older. Clinical experience in patients ≥ 75 years is very limited and deucravacitinib should be used with caution in this group of patients. *Renal Impairment:* No dose adjustment is required in patients with renal impairment, including end stage renal disease (ESRD) patients on dialysis. *Hepatic impairment:* No dose adjustment is required in patients with mild or moderate hepatic impairment. Deucravacitinib is not recommended to be used in patients with severe hepatic impairment. *Paediatric population:* The safety and efficacy of deucravacitinib in children and adolescents below the age of 18 years have not yet been established. No data are available. Method of administration: For oral use. Tablets can be taken with or without food. Tablets should be swallowed whole and should not be crushed, cut, or chewed.

CONTRAINDICATIONS: Hypersensitivity to the active substance or to any of the excipients (see SmPC). Clinically important active infections (e.g. active tuberculosis).

WARNINGS AND PRECAUTIONS: Infections: Treatment should not be initiated in patients with any clinically important active infection until the infection resolves or is adequately treated. Caution should be exercised when considering the use in patients with a chronic infection or a history of recurrent infection. Patients treated with deucravacitinib should be instructed to seek medical advice if signs or symptoms suggestive of an infection occur. If a patient develops a clinically important infection or is not responding to standard therapy, monitor carefully and deucravacitinib should not be given until the infection resolves. Pre-treatment evaluation for tuberculosis (TB): Prior to initiating treatment with deucravacitinib, patients should be evaluated

for TB infection. Deucravacitinib should not be given to patients with active TB. Treatment of latent TB should be initiated prior to administering deucravacitinib. Anti-TB therapy should be considered prior to initiation of deucravacitinib in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Patients receiving deucravacitinib should be monitored for signs and symptoms of active TB. Malignancies*: Malignancies, including lymphomas and non-melanoma skin cancer (NMSC), were observed in clinical studies with deucravacitinib. Limited clinical data are available to assess the potential relationship of exposure to deucravacitinib and the development of malignancies. Long-term safety evaluations are ongoing. The risks and benefits of deucravacitinib treatment should be considered prior to initiating patients**. Major adverse cardiovascular events (MACE), deep venous thrombosis (DVT) and pulmonary embolism (PE)*: An increased risk was not observed in clinical trials with deucravacitinib. Long-term safety evaluations are ongoing. The risks and benefits of deucravacitinib treatment should be considered prior to initiating patients**. Immunisations: Consider completion of all age-appropriate immunisations according to current immunisation guidelines prior to initiating therapy. Use of live vaccines in patients being treated with deucravacitinib should be avoided. Excipients: Contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose galactose malabsorption should not take this medicinal product. Contains less than 1 mmol of sodium (23 mg) per tablet, essentially 'sodium-free'. *serious. **It is not known whether tyrosine kinase 2 (TYK2) inhibition may be associated with the adverse reactions of Janus Kinase (JAK) inhibition. In a large randomised active-controlled study of a JAK inhibitor in rheumatoid arthritis (RA) patients 50 years and older with at least one additional cardiovascular risk factor, a higher rate of malignancies (particularly lung cancer, lymphoma and NMSC), a higher rate of MACE (defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke), and a dose dependent higher rate of venous thromboembolism (including DVT and PE) were observed with a JAK inhibitor compared to TNF inhibitors. **INTERACTIONS:** Deucravacitinib does not have any known clinically relevant drug interactions. Refer to SmPC for full details.

PREGNANCY AND LACTATION: Pregnancy: There is a limited amount of data on the use of deucravacitinib in pregnant women. As a precautionary measure, it is preferable to avoid the use of deucravacitinib during pregnancy. Breast-feeding: It is unknown whether deucravacitinib/metabolites are excreted in human milk. A risk to the newborns/infants by breast-feeding cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from deucravacitinib

therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman. Fertility: The effect of deucravacitinib on human fertility has not been evaluated.

UNDESIRABLE EFFECTS: The most commonly reported adverse reaction is upper respiratory infections (18.9%), most frequently nasopharyngitis. The longer-term safety profile of deucravacitinib was similar and consistent with previous experience. Very common (≥ 1/10): Upper respiratory infections*** (including nasopharyngitis, upper respiratory tract infection, viral upper respiratory tract infection, pharyngitis, sinusitis, acute sinusitis, rhinitis, tonsillitis, peritonsillar abscess, laryngitis, tracheitis, and rhinotracheitis). Common (≥ 1/100 to < 1/10): Herpes simplex infections*** (including oral herpes, herpes simplex, genital herpes, and herpes viral infection), Oral ulcers (including aphthous ulcer, mouth ulceration, tongue ulceration, and stomatitis), Acneiform rash (including acne, dermatitis acneiform, rash, rosacea, pustule, rash pustular, and papule), Folliculitis and Blood creatine phosphokinase increased. Uncommon (≥ 1/1000 to < 1/100): Herpes zoster***. Refer to SmPC for full details on adverse reactions.

***serious adverse drug reaction

LEGAL CATEGORY: POM

MARKETING AUTHORISATION NUMBER and BASIC NHS PRICE: PLGB 15105/0179: Carton of 28 film-coated tablets 6 mg NHS price: £690.00; Carton of 84 film-coated tablets 6 mg NHS price: £2070.00.

MARKETING AUTHORISATION HOLDER: Bristol-Myers Squibb Pharma EEIG, Plaza 254, Blanchardstown Corporate Park 2, Dublin 15, D15 T867, Ireland.

FOR FURTHER INFORMATION CONTACT:
medical.information@bms.com or 0800 731 1736 (Great Britain).

DATE OF PREPARATION: May 2023

ADDITIONAL INFORMATION AVAILABLE ON REQUEST

Approval code: 1787-GB-2300080

Adverse events should be reported. Reporting forms and information can be found at: Great Britain – www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store; Adverse events should also be reported to Bristol-Myers Squibb via medical.information@bms.com or 0800 731 1736 (Great Britain).

SOTYKTU▼ (deucravacitinib) PRESCRIBING INFORMATION

Northern Ireland / Ireland

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PRESENTATION: Film-coated tablet containing 6 mg of deucravacitinib.

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***serious adverse drug reaction

LEGAL CATEGORY: POM

MARKETING AUTHORISATION NUMBER and BASIC NHS PRICE: EU/1/23/1718/006: Carton of 28 film-coated tablets 6 mg NHS price: £690.00.

MARKETING AUTHORISATION HOLDER: Bristol-Myers Squibb Pharma EEIG, Plaza 254, Blanchardstown Corporate Park 2, Dublin 15, D15 T867, Ireland.

FOR FURTHER INFORMATION CONTACT:
medical.information@bms.com or 0800 731 1736 (Northern Ireland) / 1 800 749 749 (Ireland).

DATE OF PREPARATION: June 2023

ADDITIONAL INFORMATION AVAILABLE ON REQUEST

Approval code: 1787-IE-2300001

Adverse events should be reported. Reporting forms and information can be found at: Northern Ireland – www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store; Ireland – via HPRa Pharmacovigilance at www.hpra.ie Adverse events should also be reported to Bristol-Myers Squibb via medical.information@bms.com or 0800 731 1736 (Northern Ireland); 1 800 749 749 (Ireland).