Long-term safety of repeated cycles of rozanolixizumab treatment in patients with generalized myasthenia gravis

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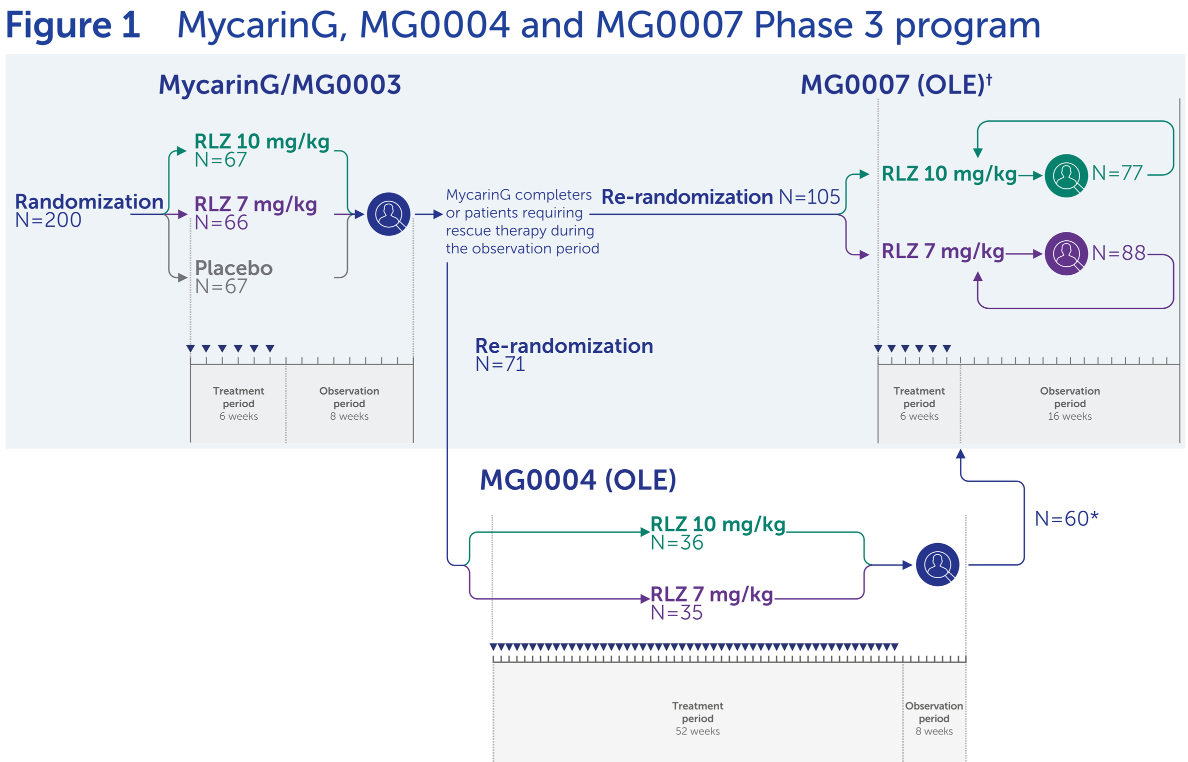
Introduction

- Rozanolixizumab is a humanized IgG4 monoclonal antibody FcRn inhibitor approved by the US FDA for the treatment of adults with AChR or MuSK Ab+ gMG[1,2]
- The MycarinG (MG0003/NCT03971422) Phase 3 study demonstrated the efficacy and safety of one 6-week cycle of rozanolixizumab in adults with gMG[1]
  — Statistically significant and clinically meaningful improvements from baseline in MG-ADL scores at Day 43 were demonstrated in rozanolixizumab-treated patients when compared with patients who received placebo
- Here, we evaluate the long-term safety of repeated rozanolixizumab treatment cycles using data pooled across MycarinG and the OLE study MG0007 (NCT04650854)

Methods

- In MycarinG, patients received weekly SC rozanolixizumab or placebo
- After completing MycarinG, patients could enroll in MG0007, in which, after an initial cycle, rozanolixizumab was administered based on symptom worsening (symptom-driven cycles) (**Figure 1**)
- Data were pooled across MycarinG and MG0007
  — Safety pool: patients with ≥1 treatment cycle (≥1 dose of rozanolixizumab in any 6-week treatment period) that was followed by a ≤8-week follow-up period across MycarinG and MG0007
- Safety outcomes included the occurrence of TEAEs and TEAEs leading to discontinuation for each 6-week treatment cycle and follow-up period
- Annualized dosing rate was calculated using the number of cycles initiated divided by time in studies (years)

Figure 1 MycarinG, MG0004 and MG0007 Phase 3 program



Data presented within this poster are from MycarinG and MG0007 only.
*Patients entering MG0007 from MG0004 continued their last dose from MG0004 for the initial cycle. †After the initial cycle, dose modifications from 10 mg/kg to 7 mg/kg and *vice versa* were permitted at the beginning of each treatment cycle provided the benefit–risk ratio remained favorable for the patient. After the initial cycle, subsequent cycles were symptom-driven (based on MG symptom worsening at the investigator's discretion, e.g. an MG-ADL score increase of ≥2.0 or a QMG score increase of ≥3.0). Patients without MG symptom worsening by the end of the observation period continued to be monitored until a further symptom-driven cycle was required.

Results

Patients

- In total, 188 patients received ≥1 cycle of rozanolixizumab 7 mg/kg (Cycle 1, n=94) or 10 mg/kg (Cycle 1, n=94) over 678 cycles and were included in the safety pool
- Baseline demographics and characteristics for patients in the safety pool are reported in **Table 1**
- Median follow-up was 368.0 days (range 44–599)
- The mean annualized dosing rate was 3.4 cycles and 17.8 SC infusions per year

Table 1 Baseline demographics and characteristics*

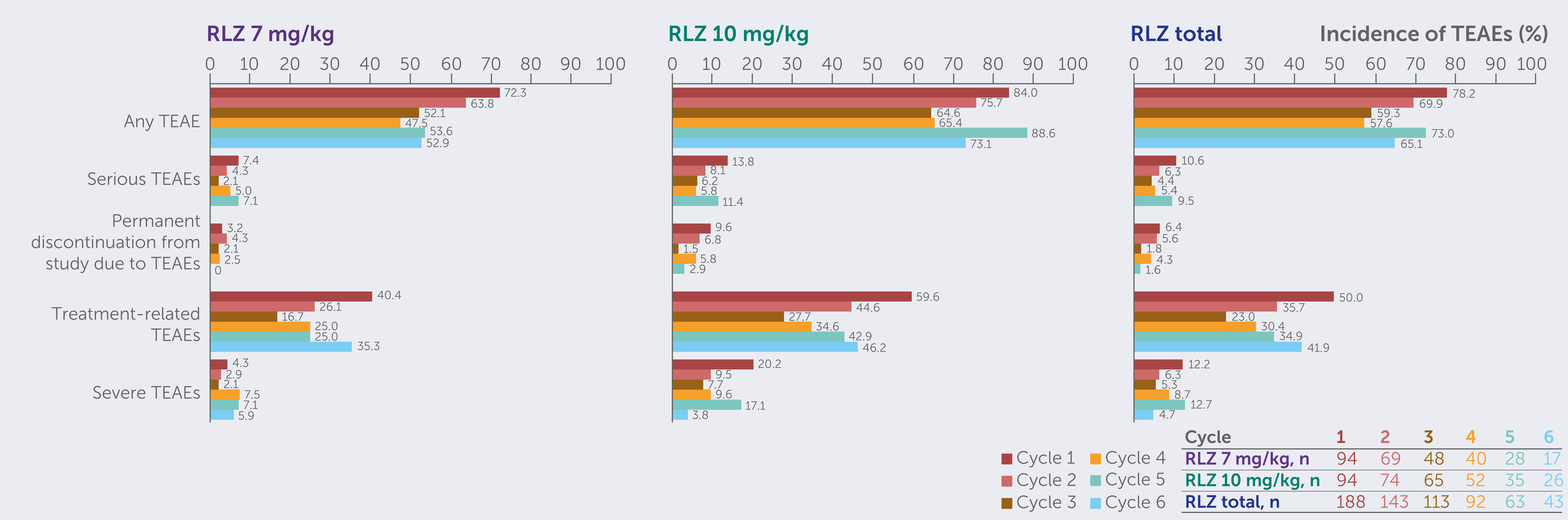
		RLZ 7 mg/kg (n=94)	RLZ 10 mg/kg (n=94)	RLZ total (N=188)
	Age, years, mean (SD)	**53.1** (14.9)	**52.0** (17.6)	**52.5** (16.3)
	Sex, female, n (%)	**56** (59.6)	**55** (58.5)	**111** (59.0)
Geographic region, n (%)	Europe	**52** (55.3)	**62** (66.0)	**114** (60.6)
	North America	**30** (31.9)	**24** (25.5)	**54** (28.7)
	Japan	**8** (8.5)	**5** (5.3)	**13** (6.9)
	Asia (excl. Japan)	**4** (4.3)	**3** (3.2)	**7** (3.7)
Race, n (%)	White	**58** (61.7)	**69** (73.4)	**127** (67.6)
	Missing†	**24** (25.5)	**11** (11.7)	**35** (18.6)
	Asian	**12** (12.8)	**9** (9.6)	**21** (11.2)
	Black	**0**	**4** (4.3)	**4** (2.1)
	Native Hawaiian or other Pacific Islander	**0**	**1** (1.1)	**1** (0.5)
	MG-ADL score, mean (SD)	**8.3** (3.7)	**8.4** (2.9)	**8.3** (3.4)

Safety pool.
*The allocation of patients to treatment group was based on the maximum dose received during the first rozanolixizumab treatment cycle, although patients may have switched rozanolixizumab doses within subsequent cycles. †Data on race were not permitted to be collected in France and Canada.

Safety

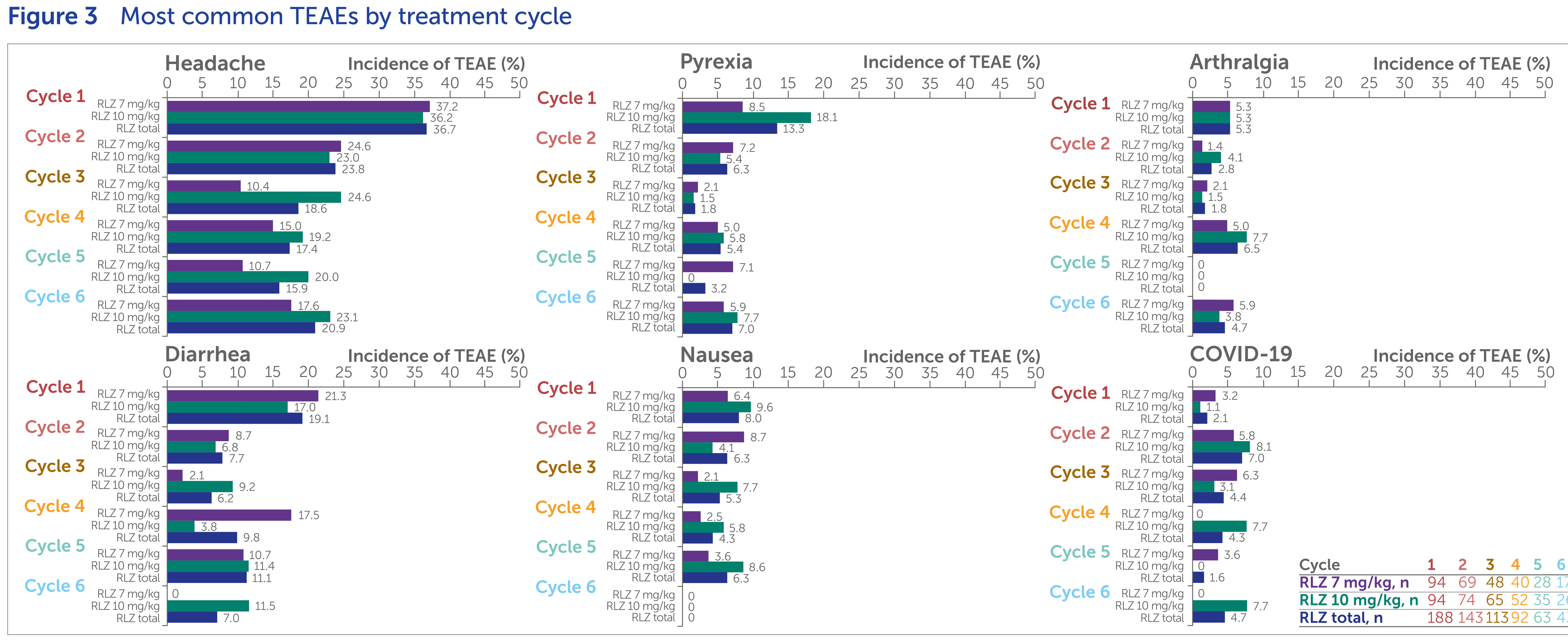
- In the safety pool, 89.9% (169/188) of patients experienced any TEAE (77.4% [103/133] of patients receiving 7 mg/kg and 91.6% [120/131] of patients receiving 10 mg/kg rozanolixizumab)[a]
  — Across all TEAE categories, the incidence of TEAEs was higher in the rozanolixizumab 10 mg/kg group than the 7 mg/kg group
  — Most TEAEs were mild or moderate in severity
- The overall incidence of TEAEs across all categories did not increase with repeated treatment cycles compared with Cycle 1 (**Figure 2**)
- Serious TEAEs occurring in >1 patient across all cycles were MG (12/188, 6.4%), MG crisis (4/188, 2.1%) and COVID-19 (3/188, 1.6%)
- Incidence of the most common TEAEs did not increase with repeated cycles of treatment (**Figure 3**)
  — Headache was the most common TEAE, predominantly of mild or moderate intensity
- TEAEs that resulted in permanent discontinuation in >1 patient were MG (5/188, 2.7%), MG crisis (2/188, 1.1%), decreased blood IgG (2/188, 1.1%) and a positive interferon gamma release assay result (2/188, 1.1%)
- There was no increase in the incidence of infections with repeated cycles of treatment. The most common infections were COVID-19, upper respiratory tract infection, nasopharyngitis and oral herpes
- There were no anaphylactic reactions. Most hypersensitivity-related events and injection-site reactions were of mild or moderate intensity and none led to permanent discontinuation
- Four deaths occurred during MG0007 due to: pneumonia caused by COVID-19 infection in two patients; pneumonia, acute kidney injury, acute respiratory failure, cardiac failure, and acute respiratory distress syndrome in one patient; and myocardial infarction in one patient (occurred >6 months after the last dose). All were deemed unrelated to rozanolixizumab by the investigator
  — One additional death occurred after data cut-off due to circulatory failure (reported as circulatory arrest) and was deemed unrelated to rozanolixizumab
- No clinically meaningful decreases in albumin concentrations or clinically relevant trends in lipid parameters were observed (data from MG0007 only)

Figure 2 Overview of TEAEs by treatment cycle



Summaries by cycle are displayed if the total number of patients undergoing the cycle in both RLZ dose groups combined was ≥10. The allocation of participants to treatment groups was according to the highest dose received during each rozanolixizumab treatment cycle.

Figure 3 Most common TEAEs by treatment cycle



The six most common TEAEs for patients across all cycles for RLZ treatment groups combined. The allocation of participants to treatment groups was according to the highest dose received during each rozanolixizumab treatment cycle.

Summary and conclusions

Pooled data are reported across MycarinG and MG0007 to assess the long term safety of repeated cycles of rozanolixizumab in adults with gMG

In general, the incidence of TEAEs did not increase with repeated treatment cycles

The majority of TEAEs were of mild or moderate intensity and non-serious

This pooled analysis demonstrates that rozanolixizumab is well tolerated with an acceptable safety profile that is consistent across repeated treatment cycles

Footnote: [a]When presenting data across all cycles, patients were assigned to the 7 mg/kg or 10 mg/kg dose group if they received the respective 7 mg/kg or 10 mg/kg dose at least once. Patients who received both 7 mg/kg and 10 mg/kg were included in both treatment groups, therefore the sum of the number of patients in the 7 mg/kg and 10 mg/kg groups is higher than the number of patients presented for rozanolixizumab total.

Abbreviations: Ab+, autoantibody-positive; AChR, acetylcholine receptor; COVID-19, coronavirus disease 2019; FcRn, neonatal Fc receptor; FDA, Food and Drug Administration; (g)MG, (generalized) myasthenia gravis; IgG, immunoglobulin G; MG-ADL, Myasthenia Gravis Activities of Daily Living; MuSK, muscle-specific tyrosine kinase; OLE, open-label extension; QMG, Quantitative Myasthenia Gravis; RLZ, rozanolixizumab; SC, subcutaneous; SD, standard deviation; TEAE, treatment-emergent adverse event.

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References: 1. Bril V, et al. Lancet Neurol. 2023;22(5):383–394. 2. Rystiggo® US PI. https://www.ucb-usa.com/RYSTIGGO-prescribing-information.pdf. Accessed August 2023.

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