INTRODUCTION

Tumor-associated macrophages (TAMs) and myeloid-derived suppressor cells are critical modulators of immune response in the tumor microenvironment.1,2 Colony-stimulating factor-1 receptor (CSF-1R) signaling drives recruitment and differentiation of TAMs, which express high levels of CSF-1R.1,2 Overall, 19 patients were treated in Part A of this study. 

METHODS

Study Design

This is a 3-part, open-label, multicenter study (NCT02880371; 35270494), sponsored by Array BioPharma Inc. The study is designed to assess the safety, tolerability, and pharmacodynamic effects of ARRY-382 on circulating monocytes and macrophages in patients with advanced solid tumors. 

Patients

Patients included adults (≥18 years of age) with advanced solid tumors. 

KEY ELIGIBILITY CRITERIA

A. Patient Eligibility

1. Patients with histologically confirmed metastatic or locally advanced malignant solid tumors with or without measurable disease. 

2. Patients with at least one previous line of systemic therapy. 

3. An ECOG PS of 0-2 or a WHO PS of 0-1. 

B. Treatment Eligibility

1. Patients who have not received a CSF-1R inhibitor in a prior clinical trial. 

C. Other Eligibility

1. Patients with a history of a known hypersensitivity to ARRY-382. 

Dose-Limiting Toxicities

2 patients in the ARRY-382 300-mg cohort experienced DLTs. 

1. Patient experienced a grade 3 rash. 

2. Patient experienced grade 3 nausea, vomiting, anorexia, and diarrhea. 

Pharmacokinetics/Pharmacodynamics

There were no evidence of PD interactions with ARRY-382 and pembrolizumab. 

CONCLUSIONS

- A total of 19 patients with various tumor types were treated. 

- Patients were heavily pretreated, with 43% having received ≥3 prior systemic regimens. 

- The DLT of ARRY-382 administered continuously on a daily basis is 300 mg QD in combination with pembrolizumab 2 mg/kg intravenously every 3 weeks. 

- ARRY-382 has a manageable safety profile. 

- The most common AEs of any grade, regardless of relationship to study drug, were increased transaminases (ALT, AST, ALP, aspartate aminotransferase, and amylase and lipase). 

- Grade 3 elevations of ALT and AST were observed and were reversible following ARRY-382 dose interruptions and, in some cases, dose reductions. 

- Immune-related AEs regardless of relationship to study drug were observed and were manageable. 

- ARRY-382 PK at the 300-mg QD dose, exposure continually exceeded the IC50 for CSF-1R inhibition in cell-based assays. 

- The maximum tolerated dose was determined to be 400 mg QD. 

- ARRY-382 plus pembrolizumab has a manageable safety profile.

REFERENCES


DISCLOSURES

The study was supported by Array BioPharma Inc.