

Supplementary Information

Title: Characterization of serous retinopathy associated with cobimetinib: Integrated safety analysis of four studies.

Journal: *Drug Safety*

Authors: Giulio Barteselli, Grant R. Goodman, Yogesh Patel, Ivor Caro, Cloris Xue, Samuel McCallum

Corresponding author: Samuel McCallum (mccallum.samuel@gene.com)

Contents

Table S1. Preferred terms used to identify SR/RPED	2
Table S2. Risk factors for SR/RPED and ocular confounders	3
Table S3. Optical coherence tomography in patients with ≥ 1 occurrence of SR in study CO39721	4

Table S1. Preferred terms used to identify SR/RPED

MedDRA Search Terms	Additional Preferred Terms
Chorioretinal disorder Chorioretinopathy Detachment of macular retinal pigment epithelium Detachment of retinal pigment epithelium Macular fibrosis Macular edema MEK inhibitor-associated serous retinopathy Retinal detachment Retinal disorder Retinal pigment epithelial tear Retinal tear Retinopathy Scleral buckling surgery Sub-retinal fluid	Foveal degeneration Macular detachment Retinal edema Serous retinal detachment Serous retinopathy

MedDRA Medical Dictionary for Regulatory Activities; *RPED* retinal pigment epithelial detachment; *SR* serous retinopathy.

Table S2. Risk factors for SR/RPED and ocular confounders

Risk factors identified from literature review	Concomitant ocular confounders
Hypertension Previous psychopharmacological medical use Antihistamine use Alcohol use Male sex Sleeping disturbances Gastroesophageal reflux disease Use of antacids or anti-reflux agents Age $\geq$ 50 years Autoimmune disease Peptic ulcer Psychological stress Obesity	Maculopathy Retinal depigmentation Macular fibrosis Age-related macular degeneration Ocular vascular disorder Retinal vascular occlusion Retinal degeneration Retinal detachment Vision blurred Chorioretinal disorder Retinal disorder Visual acuity reduced Scleral buckling surgery Macular degeneration Retinopathy hypertensive Visual impairment Macular edema Retinal pigment epitheliopathy

RPED retinal pigment epithelial detachment; *SR* serous retinopathy.

Table S3. Optical coherence tomography in patients with ≥ 1 occurrence of SR in study CO39721

OCT Findings, eyes (%)	Eyes with SR <i>n</i> = 35				
	Baseline	First SR Onset	First SR Resolution	Last SR Resolution	Last Available Visit
Any abnormal OCT finding	8 (22.9)	34 (97.1)	2 (5.7)	3 (8.6)	10 (28.6)
Subretinal fluid	–	32 (91.4)	2 (1.8)	1 (2.9)	4 (11.4)
Focal subretinal fluid	–	22 (62.9)	2 (1.8)	–	4 (11.4)
Subfoveal	–	21 (60.0)	2 (1.8)	–	4 (11.4)
Extrafoveal	–	1 (2.9)	–	–	–
Multifocal subretinal fluid	–	9 (25.7)	–	1 (0.9)	–
Subfoveal	–	2 (5.7)	–	1 (0.9)	–
Extrafoveal	–	1 (2.9)	–	–	–
Both subfoveal and extrafoveal	–	6 (17.1)	–	–	–
Normal	26 (74.3)	1 (2.9)	22 (62.9)	10 (54.3)	23 (65.7)
Missing	1 (2.9)	0	11 (31.4)	13 (37.1)	2 (5.7)

OCT optical coherence tomography; SR serous retinopathy.