Melanomas and nevi displaying regression features can be difficult to differentiate. To describe reflectance confocal microscopy features in benign and malignant pigmented skin lesions characterized by regression features in dermoscopy. Methods: Observational retrospective study. Inclusion criteria were presence of dermoscopic features of regression; availability of clinical, dermoscopic and RCM imaging; definite histopathologic diagnosis. The study sample comprised 217 lesions; 108 (49.8%) melanomas and 109 were benign lesions, of which 102 (47.0%) nevi and 7 (3.2%) lichen planus like keratosis (lplk). Patients with melanoma were significantly older than those with benign lesions (61.9±15.4 vs. 46.1±14.8; p<0.001) and a higher proportion of melanomas displayed dermoscopic regression structures in more than 50% of lesion surface (n=83/108; 76.9%; p<0.001). On RCM examination, pagetoid cells were significantly more reported in melanoma group, than in benign lesions (86.1% vs. 59.6%; p<0.001) and were more frequently widespread distributed (65.6% vs. 20.0%; p<0.001) and both dendritic and roundish (36.6% vs. 15.4%; p<0.001) in shape. Aspecific architecture at the dermo-epidermal junction (DEJ) was more commonly seen among melanomas than benign lesions (23.1% vs. 11.9%; p=0.002) with higher presence of dendritic and both dendritic and roundish atypical cells at the DEJ (28.7% vs. 18.3% and 19.4% vs. 3.7%; p<0.001, respectively). Focal pagetoid infiltration and ringed or clod patterns were more commonly seen in benign lesion. In conclusion, the correct interpretation of regressing lesions remains a challenge, assessing carefully the extent and characteristics of architectural and cytologic atypia on RCM is an additional piece of the complex puzzle of melanoma diagnosis. This article is protected by copyright. All rights reserved. KEYWORDS: dermoscopy; reflectance confocal microscopy; regression PMID: 30506970 DOI: 10.1111/exd.13853