Nisyros Island is an 8km wide Quaternary strato-volcano located at the eastern-most end of the South Aegean active volcanic arc. It hosts a 3.8km wide caldera, and is itself considered to have developed on the inferred edge of the larger submarine caldera created by the region’s largest eruption – the Kos Plateau Tuff (KPT) ~161ka. Here, we present results of a detailed study on the most recent major explosive eruptions on Nisyros (Lower and Upper Pumice) and their association with caldera formation. Lithic component analysis of xenoliths contained within the Lower and Upper Pumice pyroclastic deposits reveal circum-caldera lithic variations both temporally and spatially, and indicate that multiple vents were likely active during the caldera-forming eruptions. A possible pattern of vent-switching is suggested, which continued with the successive emplacement of post-caldera domes. Isopleth/isopach mapping is used to aid identification of vent-sites; however, it demonstrates the difficulty of such methods in very proximal environments such as Nisyros, which hosts abundant ‘hybrid’ fall/flow units and demonstrates clear evidence of multiple processes occurring simultaneously. Extensive fieldwork has lead to the construction of a new geological map and a revised volcanic stratigraphy. This relates well to our new observations of two chemically distinct magmatic series (high-Fe and low-Fe) supplying Nisyros, the interplay of which appears to influence eruptive style. Furthermore, the two series appear to correspond to distinct magmas whose mixing is suggested to have triggered the KPT eruption. Nisyros therefore seems to be part of a larger long-lived system responsible for the KPT generation.