Figure 5. Clinical Question 4 "Group 3" HER2/CEP17 ratio < 2.0 Average *HER2* signals/cell ≥ 6.0 Assess IHC using sections from the same tissue sample used for ISH IHC 0 or 1+ IHC 2+ IHC 3+ Observer blinded to previous results recounts ISH, counting at least 20 cells HER2 Negative with Comment* **HER2** Positive HER2/CEP17 ratio < 2.0 Other ISH Average *HER2* signals/cell ≥ 6.0 Result Result should be *Comment: There are insufficient adjudicated per internal **HER2** Positive data on the efficacy of HER2procedures to determine targeted therapy in cases with HER2 final category ratio < 2.0 in the absence of protein over-expression because such patients were not eligible for the first generation of adjuvant COLLEGE of AMERICAN trastuzumab clinical trials. When concurrent IHC results are negative **PATHOLOGISTS** (0-1+), it is recommended that the specimen be considered HER2 **ASCO** Guidelines negative.

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This algorithm is derived from recommendations in Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer: American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Focused Update. This is a tool based on an ASCO and CAP guideline and is not intended to substitute for the independent professional judgment of the treating physician. Practice guidelines do not account for individual variation among patients. This tool does not purport to suggest any particular course of medical treatment. Use of the guideline and this tool are voluntary.