

VENTANA anti-E-cadherin (36) Mouse Monoclonal Primary Antibody

REF

790-4497

05905290001

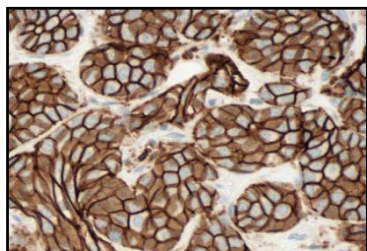
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Figure 1. VENTANA anti-E-cadherin (36) antibody staining of invasive ductal carcinoma.

INTENDED USE

VENTANA anti-E-cadherin (36) Mouse Monoclonal Primary Antibody is intended for laboratory use in qualitative immunohistochemical detection of E-cadherin by light microscopy in sections of formalin-fixed, paraffin-embedded tissue stained on a BenchMark IHC/ISH instrument. This product should be interpreted by a qualified pathologist in conjunction with histological examination, relevant clinical information, and proper controls.

This antibody is intended for in vitro diagnostic (IVD) use.

SUMMARY AND EXPLANATION

E-cadherin is a 120 kDa cell adhesion glycoprotein that functions as a calcium-dependent regulator of tight cell-cell adhesion in epithelial cells.^{1,2,3} In tumors, aberrations in E-cadherin result in the loss of cytoplasmic membrane localization of the protein and correlate with loss of adhesive properties and an increase in invasive and metastatic potential.³ Antibodies to E-cadherin have been used to characterize a variety of neoplasms, with breast applications being the most widely published.^{4,5,6}

In breast, normal ductal cells show strong membranous E-cadherin expression. In tumors of ductal origin, the pattern of E-cadherin membrane staining persists. However, tumors of lobular origin frequently exhibit aberrant E-cadherin distribution, with a high frequency having cytoplasmic or no E-cadherin reactivity, which varies with the sample cohort being evaluated and the anti-E-cadherin clone utilized.^{4,5,6} While many lobular breast carcinomas do not stain with VENTANA anti-E-cadherin (36) Mouse Monoclonal Primary Antibody (VENTANA anti-E-cadherin (36) antibody), cytoplasmic staining can be observed along with weak, partial, and punctate membrane staining. Additionally, VENTANA anti-E-cadherin (36) antibody has been shown in the literature to demonstrate a nuclear staining pattern in several tumor types.⁷ Due to the unclear clinical significance of nuclear E-cadherin staining, the pathologist should note the presence of this staining pattern and exercise caution when interpreting VENTANA anti-E-cadherin (36) antibody-stained slides. Detection of E-cadherin protein by immunohistochemistry (IHC) with the VENTANA anti-E-cadherin (36) antibody may be used to aid in the differentiation of lobular breast carcinoma from ductal breast carcinoma. It may be used as part of a panel of IHC studies.

PRINCIPLE OF THE PROCEDURE

VENTANA anti-E-cadherin (36) antibody binds to the cytoplasmic domain of the human transmembrane protein E-cadherin in formalin-fixed paraffin-embedded (FFPE) tissue sections. This antibody can be visualized using *ultraView* Universal DAB Detection Kit (Cat. No. 760-500 / 05269806001). Refer to the respective method sheet for further information.

MATERIAL PROVIDED

VENTANA anti-E-cadherin (36) antibody contains sufficient reagent for 50 tests.

One 5 mL dispenser of VENTANA anti-E-cadherin (36) antibody contains approximately 1.5 µg of a mouse monoclonal antibody.

The antibody is diluted in phosphate buffer with carrier protein and 0.10% ProClin 300, a preservative.

Specific antibody concentration is approximately 0.3 µg/mL. There is no known non-specific antibody reactivity observed in this product.

VENTANA anti-E-cadherin (36) antibody is a mouse monoclonal antibody produced from cell culture supernatant material.

Refer to the appropriate VENTANA detection kit method sheet for detailed descriptions of: Principle of the Procedure, Material and Methods, Specimen Collection and Preparation for Analysis, Quality Control Procedures, Troubleshooting, Interpretation of Results, and Limitations.

MATERIALS REQUIRED BUT NOT PROVIDED

Staining reagents, such as VENTANA detection kits and ancillary components, including negative and positive tissue control slides, are not provided.

Not all products listed in the method sheet may be available in all geographies. Consult your local support representative.

The following reagents and materials may be required for staining but are not provided:

1. Recommended control tissue
2. Microscope slides positively charged
3. Negative Control (Monoclonal) (Cat. No. 760-2014 / 05266670001)
4. *ultraView* Universal DAB Detection Kit (Cat. No. 760-500 / 05269806001)
5. Reaction Buffer Concentrate (10X) (Cat. No. 950-300 / 05353955001)
6. EZ Prep Concentrate (10X) (Cat. No. 950-102 / 05279771001)
7. LCS (Predilute) (Cat. No. 650-010 / 05264839001)
8. ULTRA LCS (Predilute) (Cat. No. 650-210 / 05424534001)
9. Cell Conditioning Solution (CC1) (Cat. No. 950-124 / 05279801001)
10. ULTRA Cell Conditioning Solution (ULTRA CC1) (Cat. No. 950-224 / 0524569001)
11. Hematoxylin II (Cat. No. 790-2208 / 05277965001)
12. Bluing Reagent (Cat. No. 760-2037 / 05266769001)
13. General purpose laboratory equipment
14. BenchMark IHC/ISH Instrument

STORAGE AND STABILITY

Upon receipt and when not in use, store at 2-8°C. Do not freeze.

To ensure proper reagent delivery and the stability of the antibody, replace the dispenser cap after every use and immediately place the dispenser in the refrigerator in an upright position.

Every antibody dispenser is expiration dated. When properly stored, the reagent is stable to the date indicated on the label. Do not use reagent beyond the expiration date.

SPECIMEN PREPARATION

Routinely processed FFPE tissues are suitable for use with this primary antibody when used with VENTANA detection kits and BenchMark IHC/ISH instruments. The recommended tissue fixative is 10% neutral buffered formalin.⁸ Sections should be cut at approximately 4 µm in thickness and mounted on positively charged slides. Slides should be stained immediately, as antigenicity of cut tissue sections may diminish over time. Ask your Roche representative for a copy of "Recommended Slide Storage and Handling" for more information.

It is recommended that positive and negative controls be run simultaneously with unknown specimens.


WARNINGS AND PRECAUTIONS

1. For in vitro diagnostic (IVD) use.
2. For professional use only.
3. **CAUTION:** In the United States, Federal law restricts this device to sale by or on the order of a physician. (Rx Only)
4. Do not use beyond the specified number of tests.
5. ProClin 300 solution is used as a preservative in this reagent. It is classified as an irritant and may cause sensitization through skin contact. Take reasonable precautions when handling. Avoid contact of reagents with eyes, skin, and mucous membranes. Use protective clothing and gloves.
6. Positively charged slides may be susceptible to environmental stresses resulting in inappropriate staining. Ask your Roche representative for more information on how to use these types of slides.
7. Materials of human or animal origin should be handled as biohazardous materials and disposed of with proper precautions. In the event of exposure, the health directives of the responsible authorities should be followed.^{9,10}

8. Avoid contact of reagents with eyes and mucous membranes. If reagents come in contact with sensitive areas, wash with copious amounts of water.
9. Avoid microbial contamination of reagents as it may cause incorrect results.
10. For further information on the use of this device, refer to the BenchMark IHC/ISH instrument User Guide, and instructions for use of all necessary components located at dialog.roche.com.
11. Consult local and/or state authorities with regard to recommended method of disposal.
12. Product safety labeling primarily follows EU GHS guidance. Safety data sheet available for professional user on request.
13. To report suspected serious incidents related to this device, contact the local Roche representative and the competent authority of the Member State or Country in which the user is established.

This product contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

Table 1. Hazard information.

Hazard	Code	Statement
	H317	May cause an allergic skin reaction.
	P261	Avoid breathing dust/ fume/ gas/ mist/ vapours/ spray.
	P272	Contaminated work clothing should not be allowed out of the workplace.
	P280	Wear protective gloves.
	P333 + P313	If skin irritation or rash occurs: Get medical advice/ attention.
	P362 + P364	Take off contaminated clothing and wash it before reuse.
	P501	Dispose of contents/ container to an approved waste disposal plant.

This product contains CAS # 55965-84-9, reaction mass of: 5-chloro-2-methyl-2H-isothiazol-3-one and 2-methyl-2H-isothiazol-3-one (3:1).

STAINING PROCEDURE

VENTANA primary antibodies have been developed for use on BenchMark IHC/ISH instruments in combination with VENTANA detection kits and accessories. Refer to the table below for recommended staining protocol.

This antibody has been optimized for specific incubation times but the user must validate results obtained with this reagent.

The parameters for the automated procedures can be displayed, printed and edited according to the procedure in the instrument User Guide. Refer to the appropriate VENTANA detection kit method sheet for more details regarding immunohistochemistry staining procedures.

For more details on the proper use of this device, refer to the inline dispenser method sheet associated with P/N 790-4497.

Table 2. Recommended staining protocol for VENTANA anti-E-cadherin (36) antibody with *ultraView* Universal DAB Detection Kit on BenchMark IHC/ISH instruments.

Procedure Type	Method	
	XT	ULTRA or ULTRA PLUS ^a
Deparaffinization	Selected	Selected
Cell Conditioning (Antigen Unmasking)	CC1, Standard	ULTRA CC1, 64 minutes, 95°C
Antibody (Primary)	16 minutes, 37°C	24 minutes, 36°C
Counterstain	Hematoxylin II, 4 minutes	
Post Counterstain	Bluing, 4 minutes	

^aConcordance was demonstrated between BenchMark ULTRA and BenchMark ULTRA PLUS instruments using representative assays.

Due to variation in tissue fixation and processing, as well as general lab instrument and environmental conditions, it may be necessary to increase or decrease the primary antibody incubation, cell conditioning or protease pretreatment based on individual specimens, detection used, and reader preference. For further information on fixation variables, refer to "Immunohistochemistry Principles and Advances."¹¹

NEGATIVE REAGENT CONTROL

In addition to staining with VENTANA anti-E-cadherin (36) antibody, a second slide should be stained with the appropriate negative control reagent.

POSITIVE TISSUE CONTROL

Optimal laboratory practice is to include a positive control section on the same slide as the test tissue. This helps identify any failures applying reagents to the slide. Tissue with weak positive staining is best suited for quality control. Control tissue may contain both positive and negative staining elements and serve as both the positive and negative control. Control tissue should be fresh autopsy, biopsy, or surgical specimen, prepared or fixed as soon as possible in a manner identical to test sections.

Known positive tissue controls should be utilized only for monitoring performance of reagents and instruments, not as an aid in determining specific diagnosis of test samples. If the positive tissue controls fail to demonstrate positive staining, results of the test specimen should be considered invalid.

An example of positive control tissue for this antibody is ductal breast carcinoma. Positive staining in tumor cells should be similar to normal expression level observed in ducts of the breast.

STAINING INTERPRETATION / EXPECTED RESULTS

The expected cellular staining pattern for VENTANA anti-E-cadherin (36) antibody is membranous.

SPECIFIC LIMITATIONS

While cytoplasmic or nuclear staining may be seen with VENTANA anti-E-cadherin (36) antibody, the clinical significance of this expression pattern is unclear and pathologists should exercise caution and interpret membranous E-cadherin staining only.

All assays might not be registered on every instrument. Please contact your local Roche representative for more information.

PERFORMANCE CHARACTERISTICS

ANALYTICAL PERFORMANCE

Staining tests for sensitivity, specificity, and precision were conducted and the results are listed below.

Sensitivity and Specificity

Table 3. Sensitivity/Specificity of VENTANA anti-E-cadherin (36) antibody was determined by testing FFPE normal tissues.

Tissue	# positive / total cases	Tissue	# positive / total cases
Cerebrum	0/3	Esophagus	3/3
Cerebellum	0/3	Stomach	3/3
Adrenal gland	0/3	Small intestine	3/3
Ovary	0/3	Colon	2/3
Pancreas	3/3	Liver	3/3
Parathyroid gland	3/3	Salivary gland	3/3
Pituitary gland	3/3	Kidney	3/3
Testis	0/3	Prostate	3/3
Thyroid	3/3	Bladder	3/3
Breast ^a	18/18	Endometrium	3/3

Tissue	# positive / total cases	Tissue	# positive / total cases
Spleen	3/3	Cervix	3/3
Tonsil	3/3	Skeletal muscle	0/3
Thymus	0/3	Skin	3/3
Bone marrow	0/3	Nerve	0/3
Lung	0/3	Mesothelium	0/3
Heart	0/3		

^a Tissue includes normal, adenosis and fibrocystic changes

Table 4. Sensitivity/Specificity of VENTANA anti-E-cadherin (36) antibody was determined by testing a variety of FFPE neoplastic tissues.

Pathology	# positive / total cases
Glioblastoma (Cerebrum)	0/1
Meningioma (Cerebrum)	1/1
Ependymoma (Cerebrum)	0/1
Oligodendroglioma (Cerebrum)	0/1
Serous adenocarcinoma (Ovary)	1/1
Mucinous adenocarcinoma (Ovary)	1/1
Neuroendocrine neoplasm (Pancreas)	0/1
Adenocarcinoma (Pancreas)	1/1
Seminoma (Testis)	1/1
Embryonal carcinoma (Testis)	0/1
Medullary carcinoma (Thyroid)	1/1
Papillary carcinoma (Thyroid)	1/1
Paget's Disease (Breast)	1/1
Lobular carcinoma in situ (Breast)	2/2
Ductal carcinoma in situ (Breast)	40/40
Invasive ductal carcinoma (Breast)	199/204
Invasive lobular carcinoma (Breast) ^a	31/60
Mixed ductal and lobular carcinoma (Breast)	2/2
Invasive micropapillary carcinoma (Breast)	1/1
Fibroadenoma (Breast)	10/10
Mucinous adenocarcinoma (Breast)	8/9
Papillary carcinoma (Breast)	2/2
Squamous cell carcinoma (Breast)	1/1
Clear cell carcinoma (Breast)	1/1
Small cell carcinoma (Lung)	1/1
Squamous cell carcinoma (Lung)	1/1
Adenocarcinoma (Lung)	1/1

Pathology	# positive / total cases
Squamous cell carcinoma (Esophagus)	1/1
Adenocarcinoma (Esophagus)	1/1
Mucinous adenocarcinoma (Stomach)	0/1
Adenocarcinoma (Small intestine)	1/1
Gastrointestinal stromal tumor (Small intestine)	0/1
Adenocarcinoma (Colon)	1/1
Gastrointestinal stromal tumor (Colon)	0/1
Adenocarcinoma (Rectum)	1/1
Gastrointestinal stromal tumor (Rectum)	0/1
Hepatocellular carcinoma (Liver)	1/1
Hepatoblastoma (Liver)	0/1
Clear cell carcinoma (Kidney)	0/1
Adenocarcinoma (Prostate)	1/1
Urothelial carcinoma (Prostatic urethra)	1/1
Leiomyoma (Uterus)	0/1
Adenocarcinoma (Uterus)	1/1
Clear cell carcinoma (Uterus)	1/1
Squamous cell carcinoma (Cervix)	2/2
Embryonal rhabdomyosarcoma (Striated muscle)	0/1
Basal cell carcinoma (Skin)	0/1
Squamous cell carcinoma (Skin)	1/1
Neurofibroma (Lumbar)	0/1
Neuroblastoma (Retroperitoneum)	0/1
Spindle cell rhabdomyosarcoma (Peritoneum)	0/1
Mesothelioma	1/1
Lymphoma, NOS	0/2
B-cell lymphoma, NOS	0/2
Hodgkin lymphoma	0/1
Urothelial carcinoma (Bladder)	1/1
Leiomyosarcoma	0/2
Osteosarcoma (Bone)	0/1

^a 22/31 cases of invasive lobular carcinoma that stained with VENTANA anti-E-cadherin (36) antibody, displayed fragmented membranous expression which is consistent with published literature; invasive lobular carcinoma may display fragmented, focal, dot-like, or aberrant membranous E-cadherin expression.¹²

Precision

Precision studies for VENTANA anti-E-cadherin (36) antibody were completed to demonstrate:

- Between-lot intermediate precision of the antibody.
- Within-run and between-day precision on a BenchMark XT instrument.
- Between-instrument precision on the BenchMark XT and BenchMark ULTRA instruments.
- Between-platform precision between the BenchMark XT and BenchMark ULTRA instruments.

All studies met their acceptance criteria.

Precision on the BenchMark ULTRA PLUS instrument was demonstrated using representative assays. Studies included Within-run Repeatability, Between-day and Between-run Intermediate Precision. All studies met their acceptance criteria.

CLINICAL PERFORMANCE

Clinical performance data relevant to the intended purpose of VENTANA anti-E-cadherin (36) antibody were assessed by systematic review of the literature. The data gathered support the use of the device in accordance with its intended purpose.

REFERENCES

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NOTE: A point (period/stop) is always used in this document as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

The summary of safety and performance can be found here:

<https://ec.europa.eu/tools/eudamed>

Symbols

Ventana uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see [dialog.roche.com](https://www.dialog.roche.com) for definition of symbols used):



Global Trade Item Number



Unique Device Identification



Indicates the entity importing the medical device into the European Union

REVISION HISTORY

Rev	Updates
D	<p>Updates to Intended Use, Summary and Explanation, Principle of the Procedure, Material Provided, Materials Required but not Provided, Storage and Stability, Specimen Preparation, Warnings and Precautions, Staining Procedure, Negative Reagent Control, Positive Tissue Control, Staining Interpretation / Expected Results, Specific Limitations, Analytical Performance, Clinical Performance, References, Symbols, Intellectual Property, and Contact Information sections.</p> <p>Added BenchMark ULTRA PLUS instrument.</p> <p>Removed recommended protocols for iVIEW DAB detection kit.</p>

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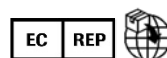
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