Case presentation:

Hamideh sadat mirmohammadi

Pediatric hematology-oncology fellow
Iran University of Medical Sciences

Introduction :

A 9-year-old boy who had been experiencing :

- ✓ progressive hoarseness
- ✓ recurrent upper respiratory symptoms
- ✓ nocturnal snoring
- ✓ episodes of obstructive sleep apnea

Since April 2023…

During this period , the patient had been receiving outpatient treatments with the diagnoses of sinusitis , allergy and others.

Despite initial conservative management,
there was no clinical improvement,
prompting referral for further diagnostic work-up.

With referral to an otolaryngologist and thorough examination, a tissue was removed during the examination and sent for pathology. Then Flexible laryngoscopy was performed, revealing a mass in the supraglottic larynx.

IHC results on block, NO:3969

CD34: Negative

CK7: Negative

Vimentin : Positive

S100: Negative

Desmin: Negative

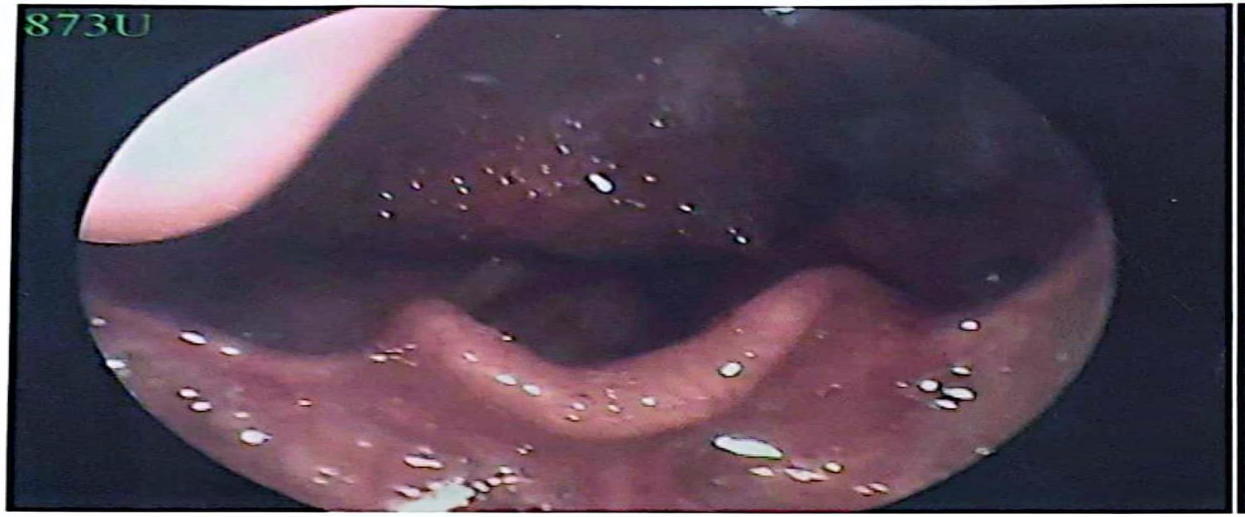
Myogenin : Negative

CD99: Positive diffusely

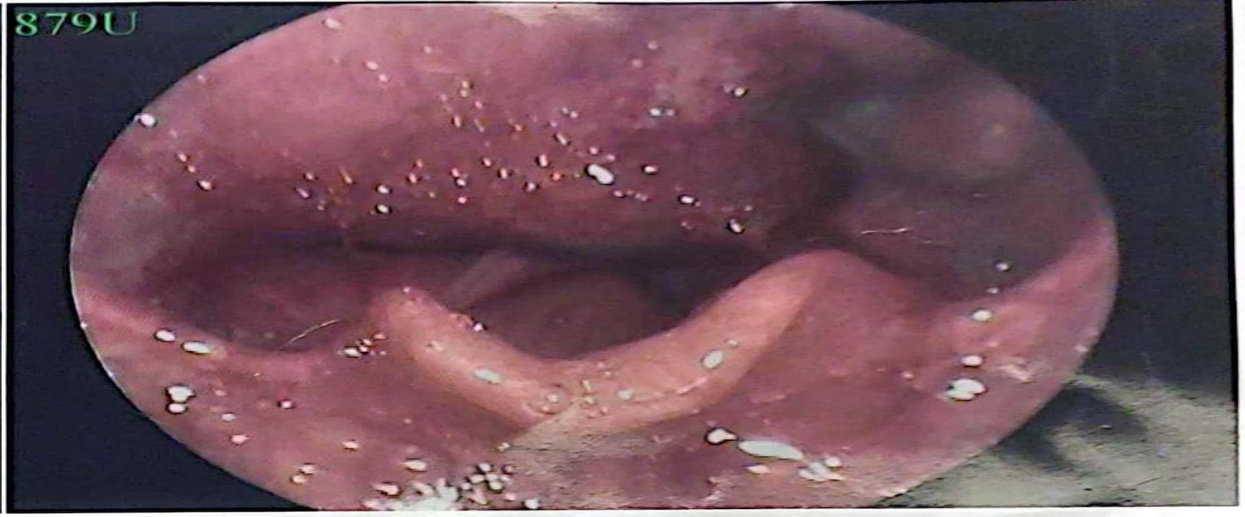
CK: Negative

CD45: Negative

These IHC result on laryngeal mass are in favor of Ewing sarcoma /primitive neuroectodermal tumor (EWS/ PNET)



Lx



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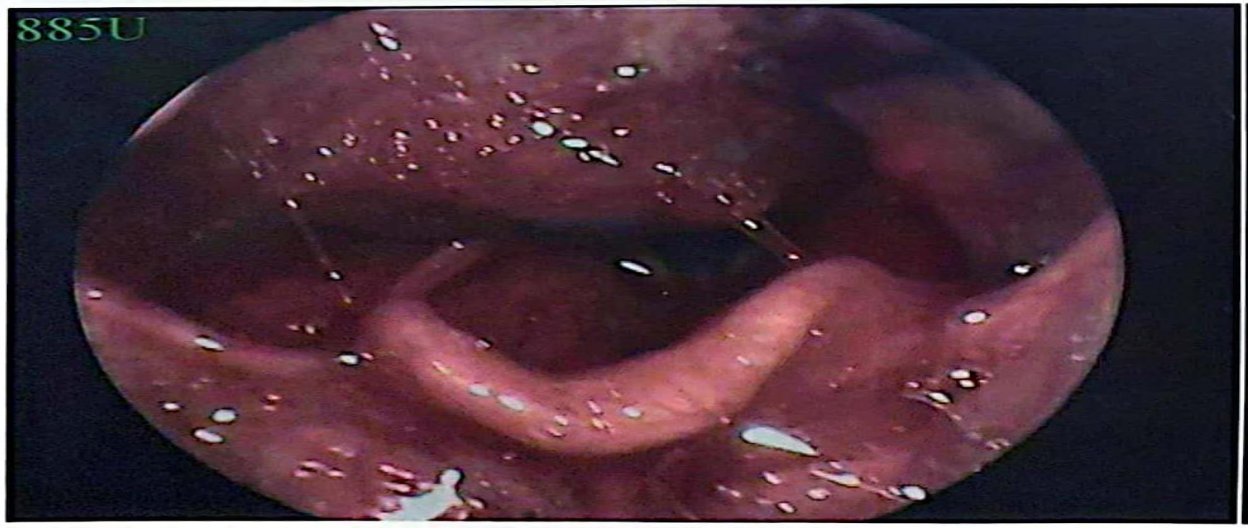
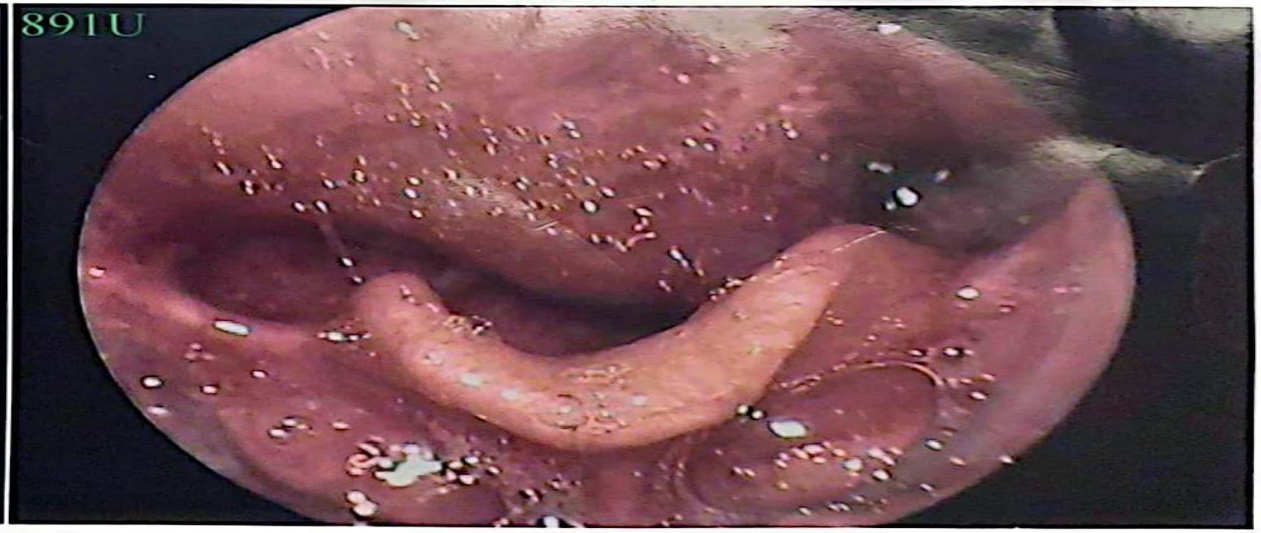




In June 2024, the patient was admitted to Ali Asghar Children’s Hospital

with a presumptive diagnosis of primitive neuro ectodermal tumor (PNET), and empirical chemotherapy was initiated based on this working diagnosis.

Imaging at the time of diagnosis,
including MRI and CT of the neck,
revealed a well-defined enhancing mass
measuring approximately 51×37 mm,
centered in the right larynx and hypopharynx.

The lesion extended superiorly into the supra glottic
space and inferiorly toward the right arytenoid and
cricoid cartilages, with possible involvement of
the thyroid cartilage, although no invasion of
the vocal cords or surrounding soft tissues
was noted.

At this stage,initial evaluation including chest and abdominal ct scan and pet scan were performed to assess for potential involvement in other parts of the body.

All investigations revealed no additional sites of involvement, and no evidence of metastasis was detected.

The patient was subsequently referred for surgery,
and a surgical biopsy with partial excision of the mass were successfully performed.

Histopathological evaluation of the
excised specimen revealed
a spindle cell neoplasm.

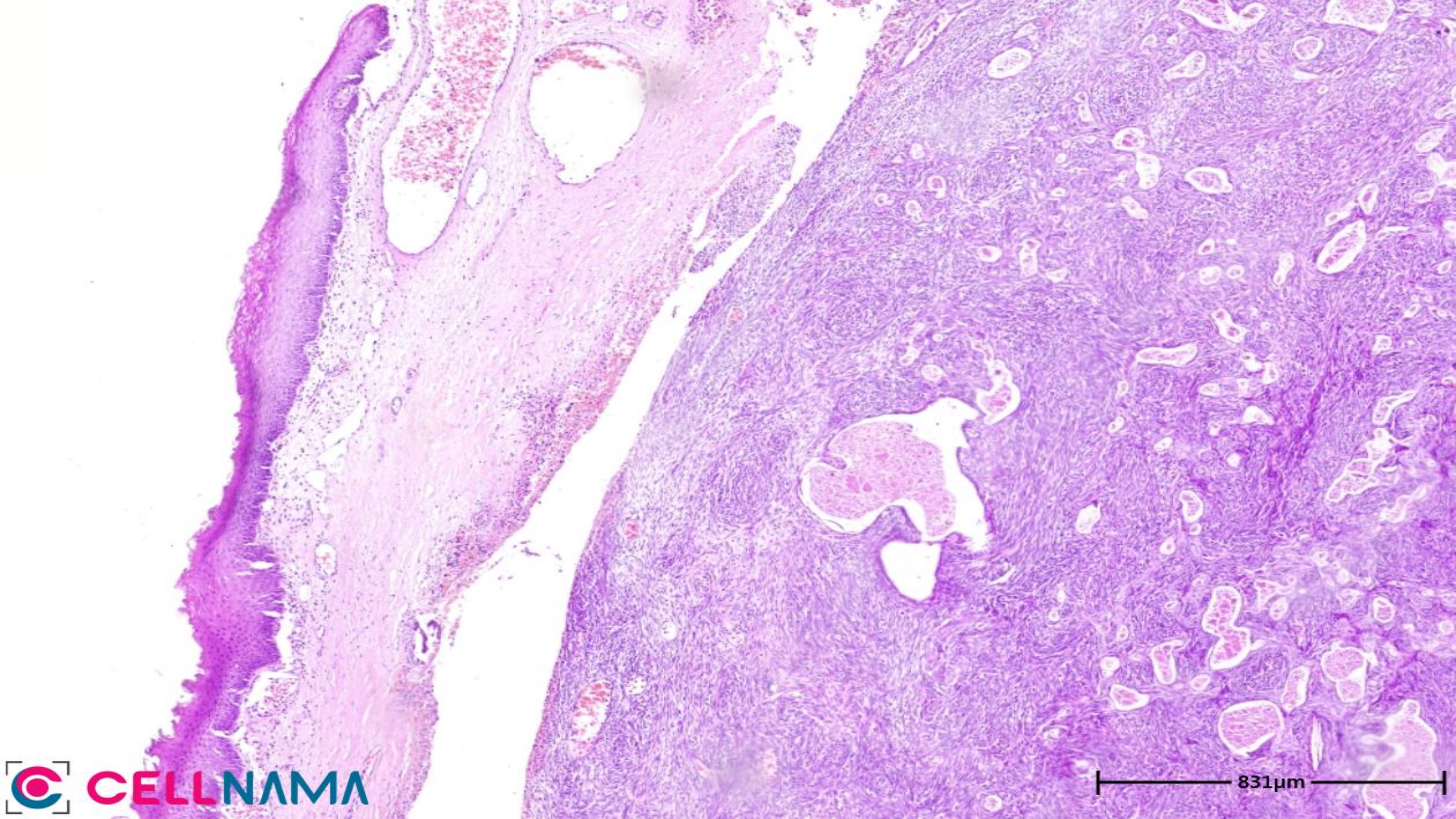
Immunohistochemical (IHC) analysis
demonstrated strong nuclear expression of
TLE1, diffuse cytoplasmic positivity for Vimentin,
and a Ki-67 proliferation index
of approximately 50%,
reflecting a high mitotic rate.

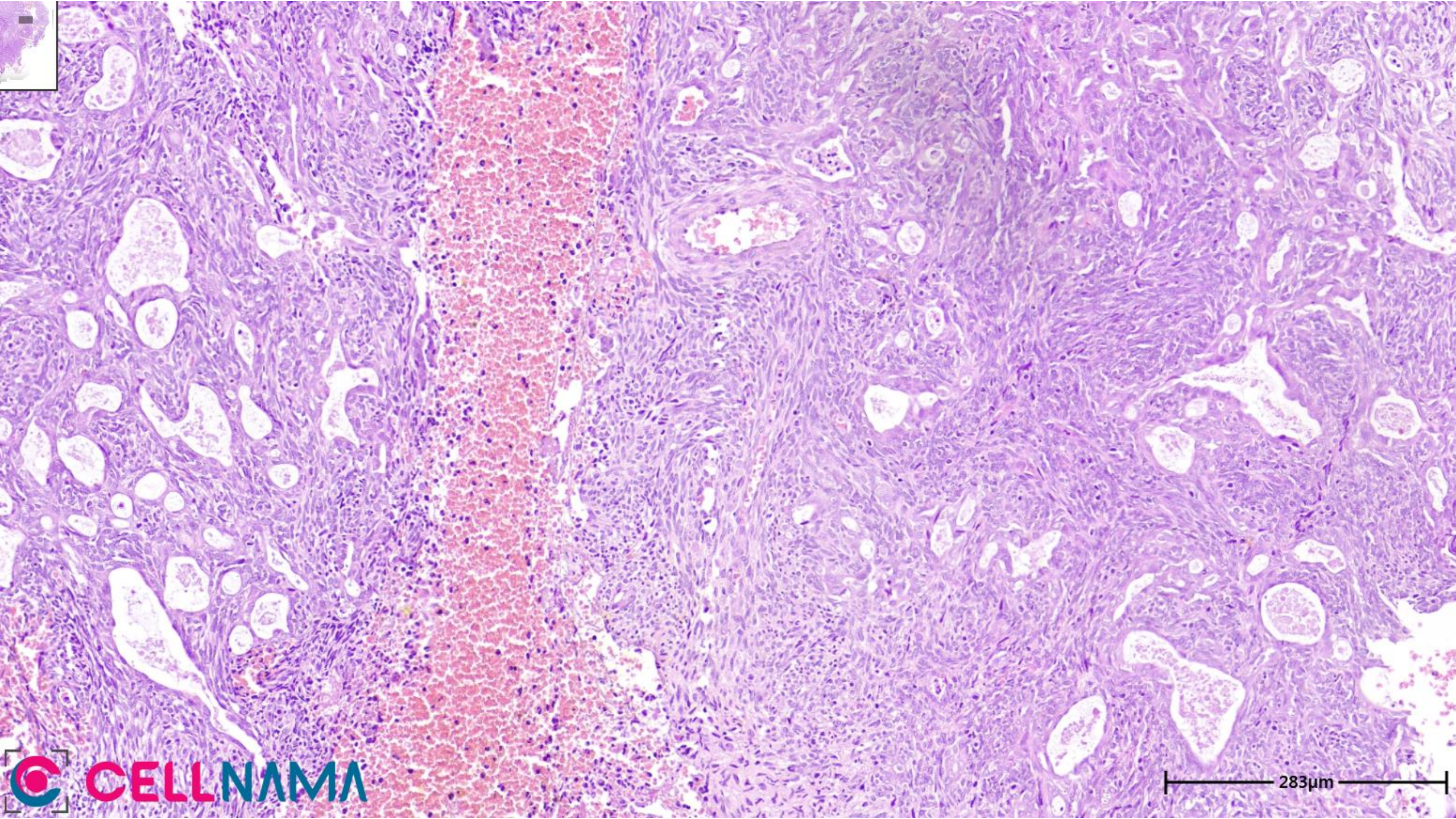
Additional IHC markers were positive for CD99, EMA, BCL-2, and CK, and negative for S100, SOX10, CD117, CD34, SMA, Desmin,and P63, thereby excluding several differential diagnoses, including rhabdomyosarcoma, lymphoma, and other soft tissue sarcomas.

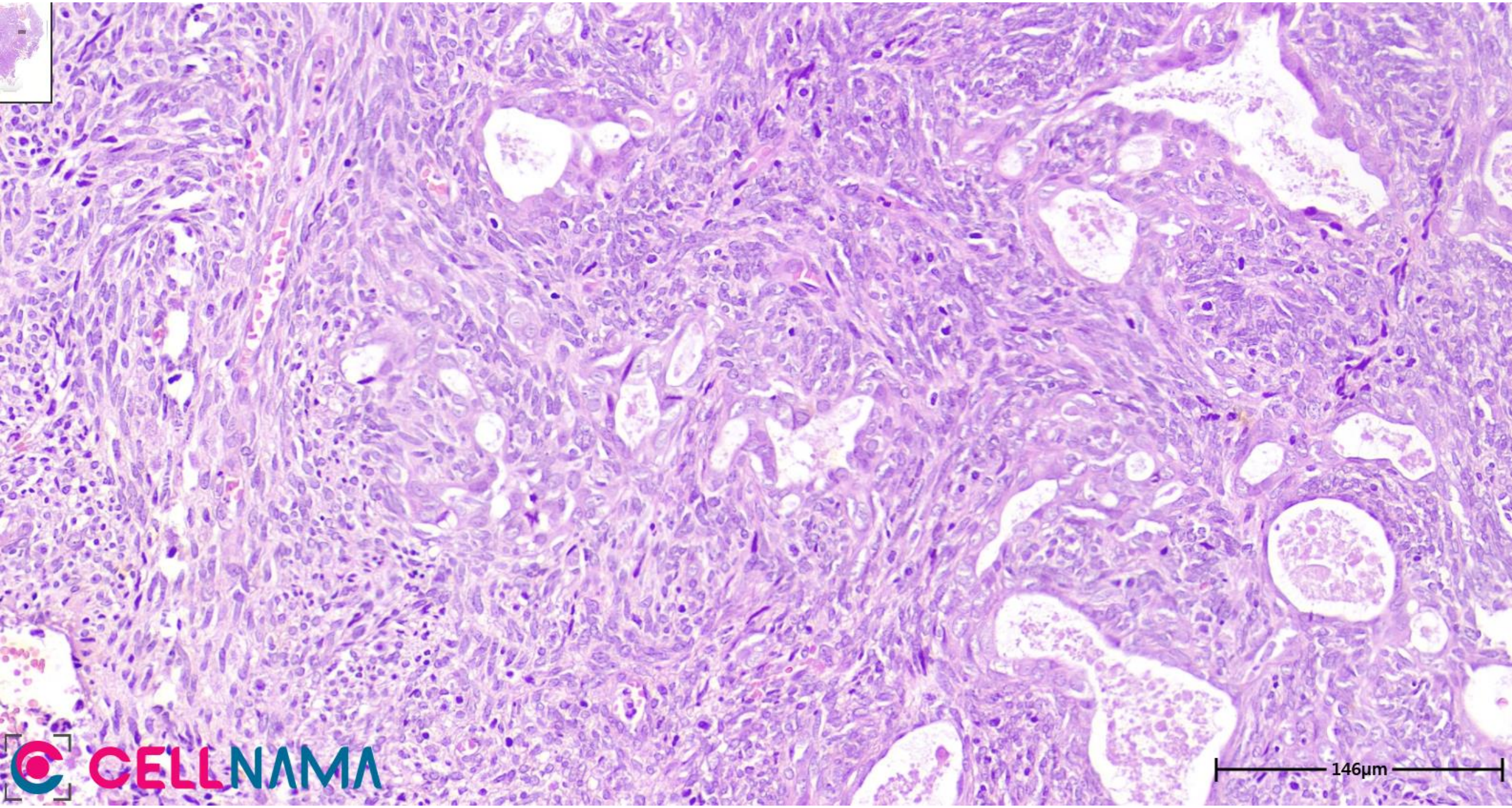
Morphologic study
and
IHC staining are
more In favor of
Synovial sarcoma/biphasic spindle cell variant.

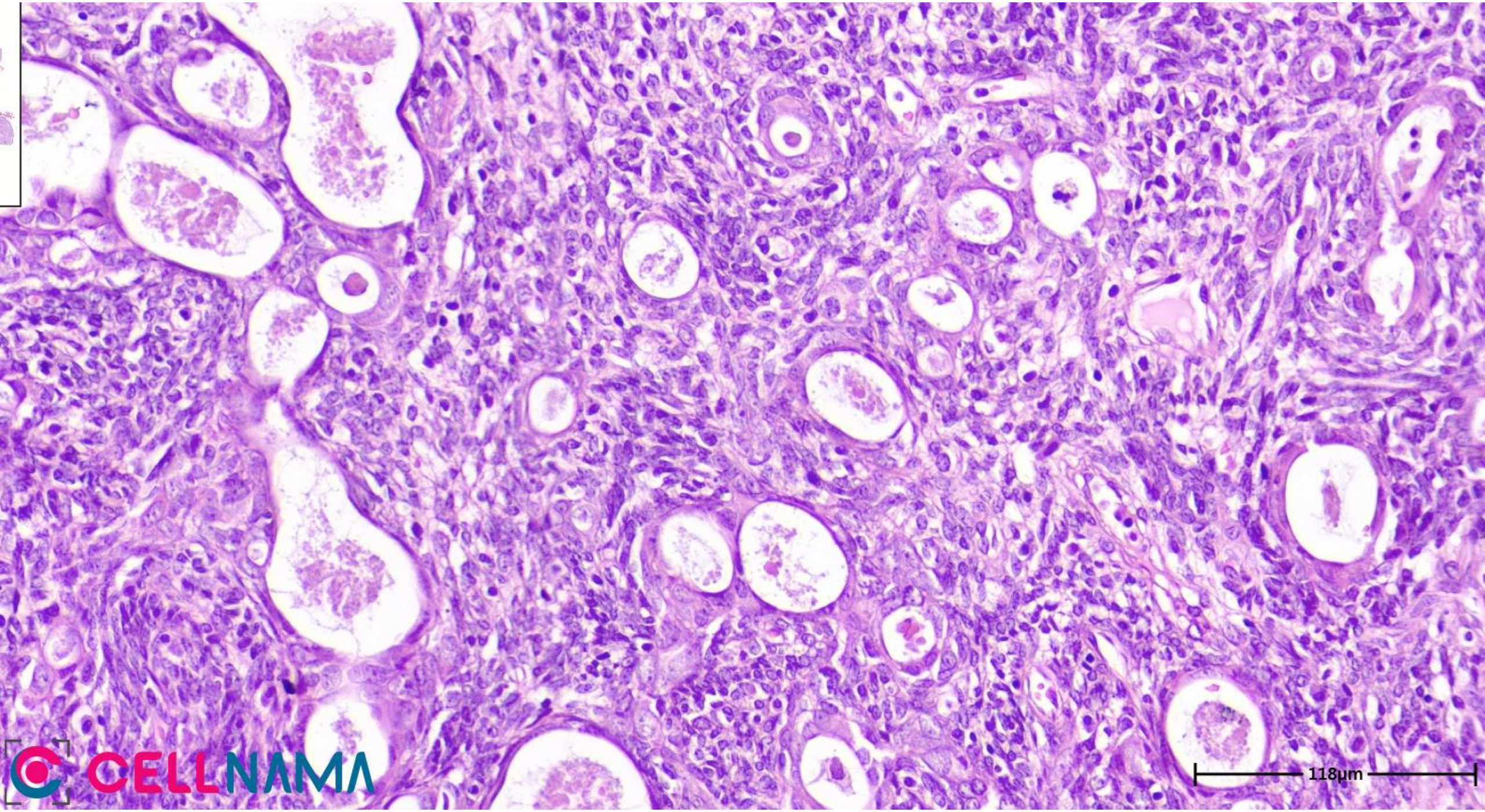
Further molecular characterization via FISH confirmed the presence of SS18 gene rearrangement, establishing the diagnosis of biphasic synovial sarcoma.

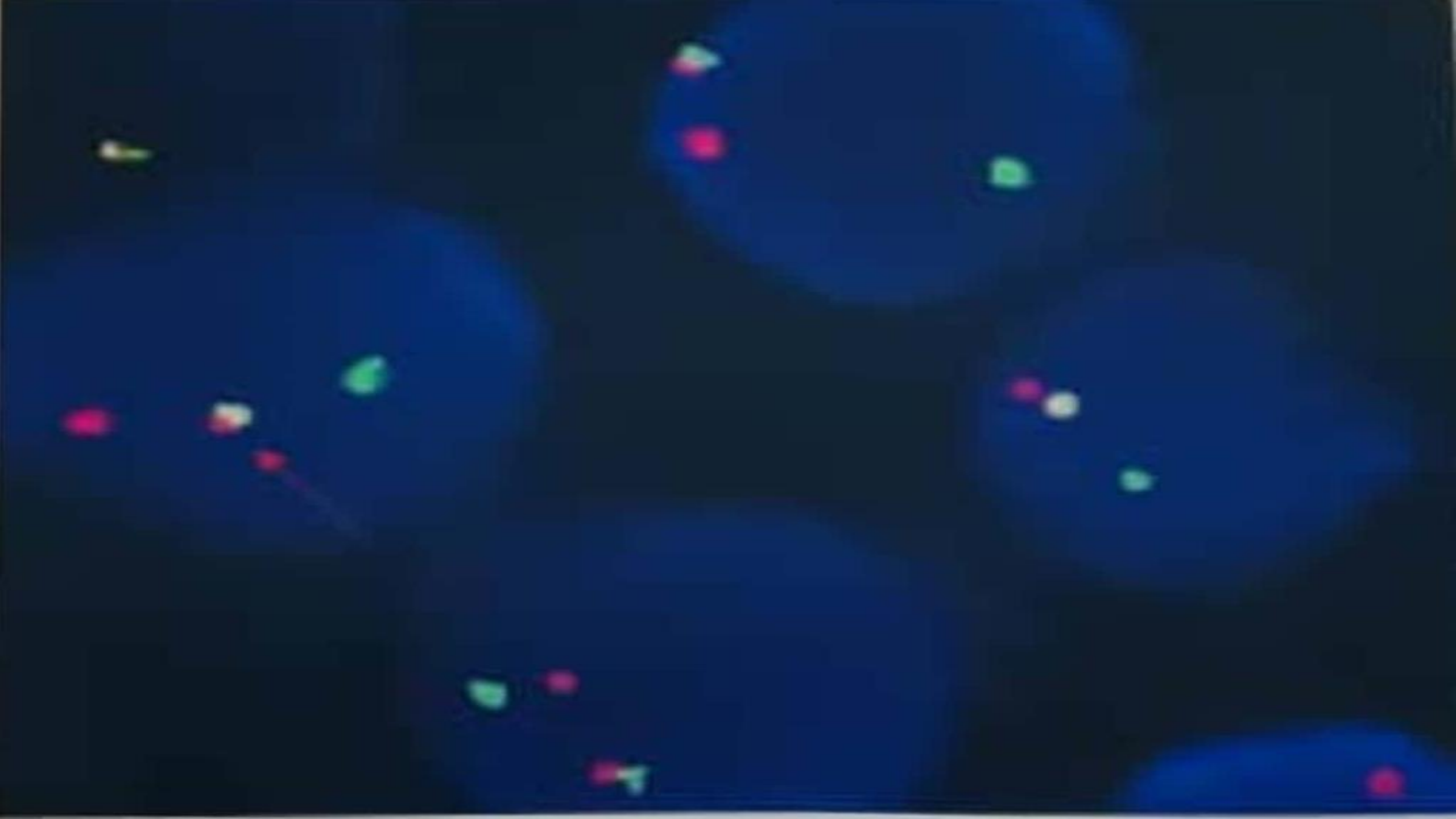
Additional testing for EML4-ALK fusion was negative, and PD-L1 expression was minimal (Tumor Proportion Score <5%).


831µm


CELLNAMA
283µm


CELLNAMA
146µm


CELLNAMA
118µm



Following the confirmed diagnosis,
the patient underwent multimodal treatment.

This included six cycles of ID chemotherapy,
followed by 30 sessions of external beam radiotherapy,
targeting the primary tumor site.

At the completion of the chemotherapy protocol and based on the subsequent evaluations,
given the residual primary tumor tissue with slight enhancement and
with a suspicious finding on pet scan
further treatment was administered with four courses of irinotecan and temozolomide in combination with immunotherapy using ipilimumab and nivolumab.

Treatment response was evaluated
through serial imaging studies.

A post-treatment FDG PET/CT performed
in January 2025 showed
no evidence of hypermetabolic activity,
consistent with a complete metabolic response.

Nevertheless, a residual lesion measuring
12×8×7 mm was identified
in the right supraglottic region,
adjacent to the right thyroid cartilage,
on MRI scans in both December 2024 and May 2025.

The lesion remained stable in size and morphology and was interpreted as either post-therapeutic fibrotic tissue or metabolically inactive residual tumor.

No lymphadenopathy or signs of distant spread were observed on follow-up imaging.

As of the most recent follow-up,
the patient remains clinically stable,
asymptomatic,
and is under active surveillance with
periodic MRI and PET/CT studies.

Imaging findings to date support
sustained remission and
indicate an excellent therapeutic response.

Synovial sarcoma

- ✓ Synovial sarcoma is the most common NRSTS in children and adolescents, accounting for 7.9% of pediatric STS but only 2.2% of STS among adults.

- ✓ Despite the reported incidence, laryngeal synovial sarcoma in children is extremely rare, with only about nine cases reported in the pediatric age group between 1988 and 2024.

- ✓ The median at diagnosis is 12 years
- ✓ The SS18-SSX1 and SS18-SSX2 transcripts can be detected in more than 90% of synovial sarcomas.
- ✓ Two histologic subtypes, the more common monophasic spindle cell morphology subtype and a biphasic subtype.
- ✓ In pediatric patients, large tumor size, unresectable tumor, and metastatic disease have been identified as unfavorable features.

- ✓ Wide local excision
- ✓ RT preoperatively or postoperatively
- ✓ Chemotherapy

What is novel?

DIAGNOSTIC PATHWAY AND CHALLENGES :

The introduction of better diagnostic IHC markers and the use of molecular assays for gene translocation, such as FISH, may help diagnose SS more rapidly. Recently, SS fusion protein-specific IHC has shown promise as a diagnostic tool.

DIAGNOSTIC PATHWAY AND CHALLENGES :

The SS18:SSX fusion-specific antibody,
E9X9V, was designed to bind to the fusion protein
at the fusion junction and demonstrated
high sensitivity and specificity for SS.

A second antibody, E5A2C,
which is targeted to the SSX C terminus, showed high sensitivity,
but was slightly less specific than E9X9V for SS.

FUTURE PERSPECTIVES ON SYNOVIAL SARCOMA TREATMENT :

Agents directed at the following targets are under investigation:

- vascular endothelial growth factor receptors,
- platelet-derived growth factor receptors,
- mitogen-activated protein kinases,
- the receptor TK c-Kit,
- the enhancer of zeste homolog 2 (EZH2),
- the raptor-mammalian target of rapamycin (mTOR) complex 1/rictor-mTOR complex (mTORC1/2),
- the chromatin-binding regulatory protein BRD9,
- and neural cell adhesion molecule CD56.

FUTURE PERSPECTIVES ON SYNOVIAL SARCOMA TREATMENT :

Among agents directed against these targets,
a phase II study showed that tazemetostat,
an oral selective EZH2 inhibitor,
was well tolerated but showed
marginal clinical activity in patients with SS.

munohistochemical expression :

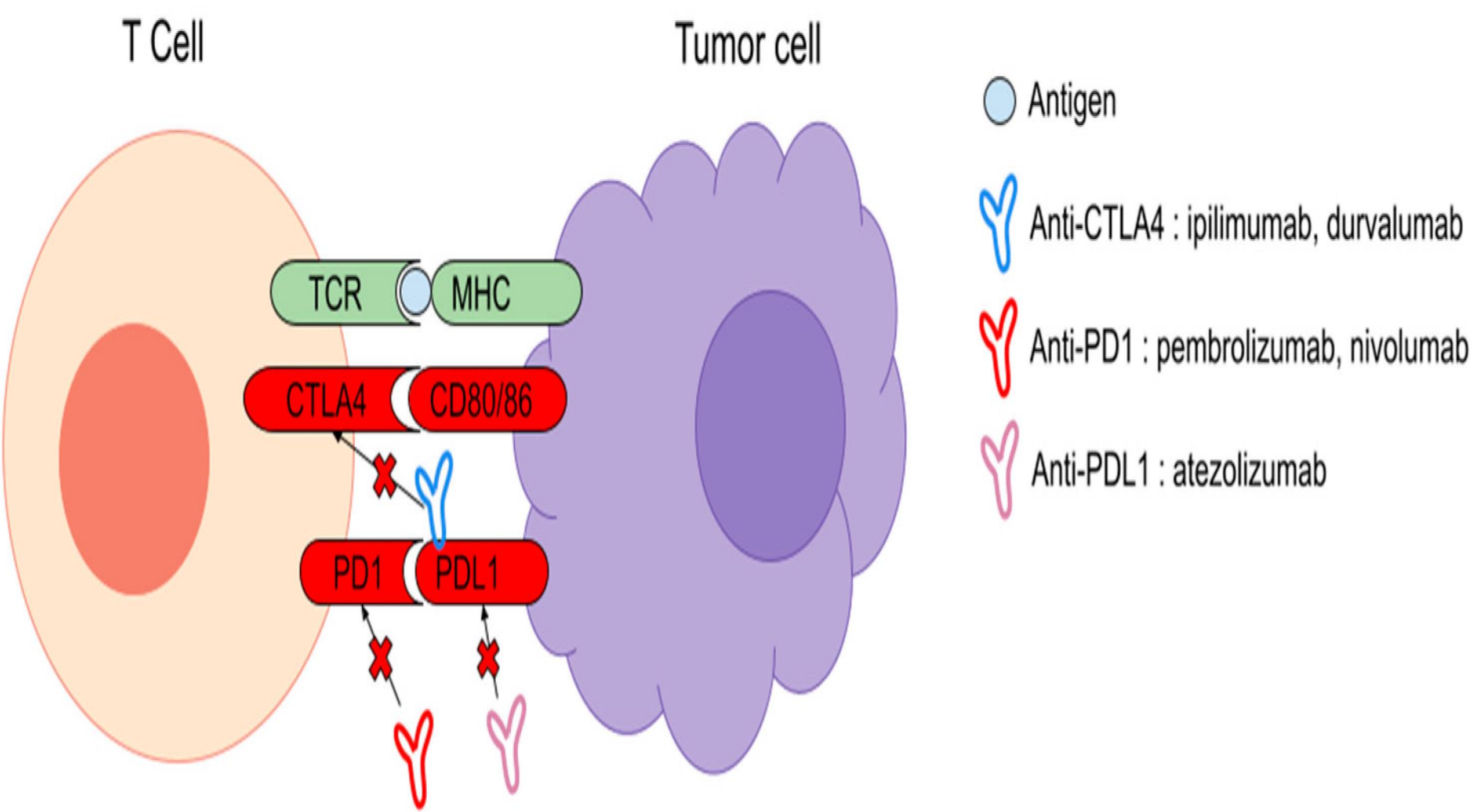
PD-1,PD-L1

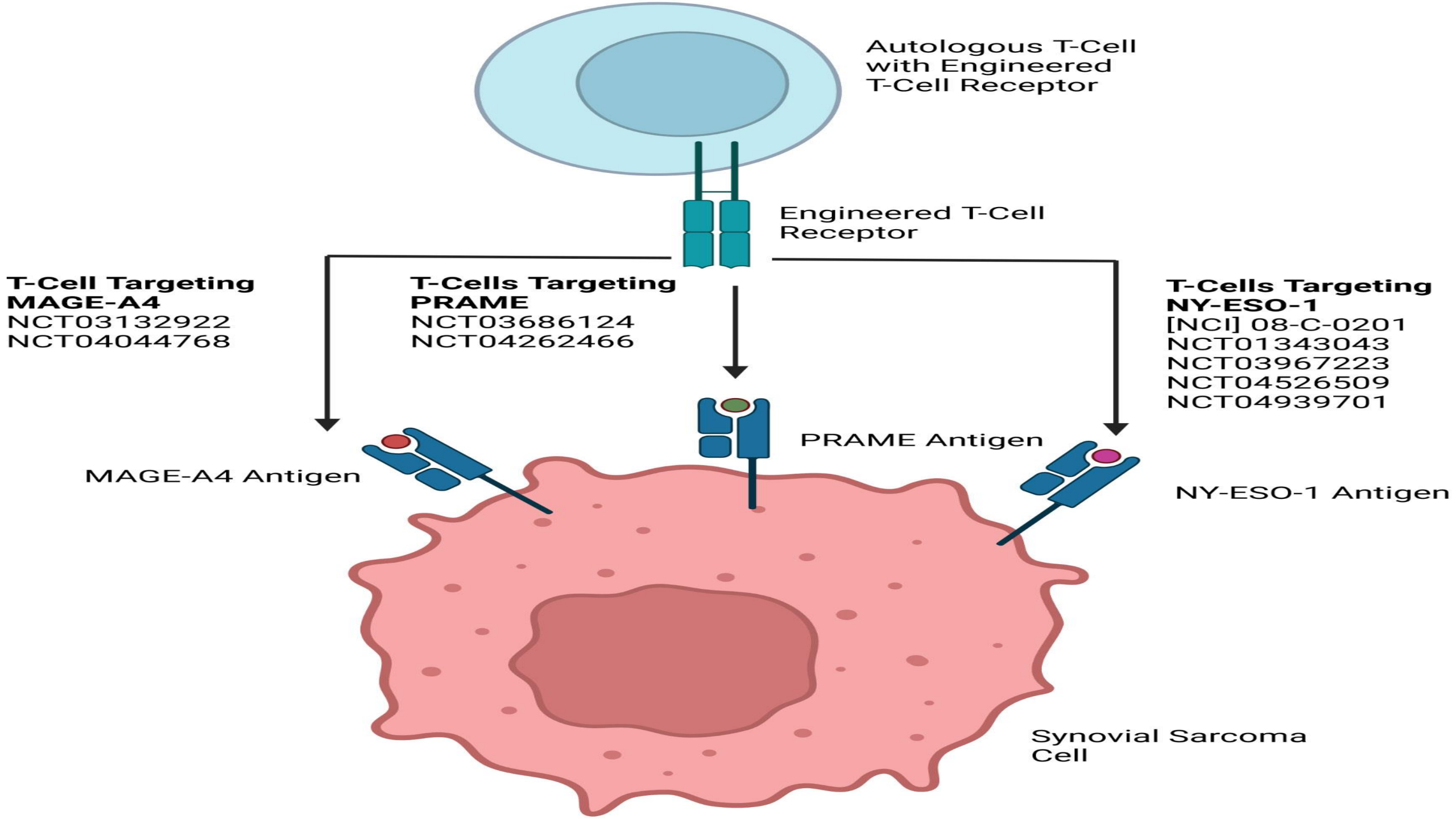
CTLA-4

NY-ESO-1,MAGE-A4,PRAME

Table 4. CTA expression of interest in SS and associated TCR T-cell therapies under investigation

CTA	Expression in SS	CTA detection method	CTA-targeted TCR T-cell therapy	References
MAGE-A4	53%-82%	IHC	Afami-cel	9,42,100,101
NY-ESO-1	70%-80%	IHC	Lete-cel	84,91,97,102
PRAME	100%	IHC or PCR	IMA203	43,100,103


T Cell
Tumor cell
TCR
MHC
CTLA4
CD80/86
PD1
PDL1
Antigen
Anti-CTLA4 : ipilimumab, durvalumab
Anti-PD1 : pembrolizumab, nivolumab
Anti-PDL1 : atezolizumab


Autologous T-Cell
with Engineered
T-Cell Receptor
Engineered T-Cell
Receptor
T-Cell Targeting
MAGE-A4
NCT03132922
NCT04044768
T-Cells Targeting
PRAME
NCT03686124
NCT04262466
T-Cells Targeting
NY-ESO-1
[NCI] 08-C-0201
NCT01343043
NCT03967223
NCT04526509
NCT04939701
PRAME Antigen
MAGE-A4 Antigen
NY-ESO-1 Antigen
Synovial Sarcoma
Cell

Thanks For Your attention