Post Renal Transplant Malignancy

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KUWAIT - 8/2/2026

Agenda

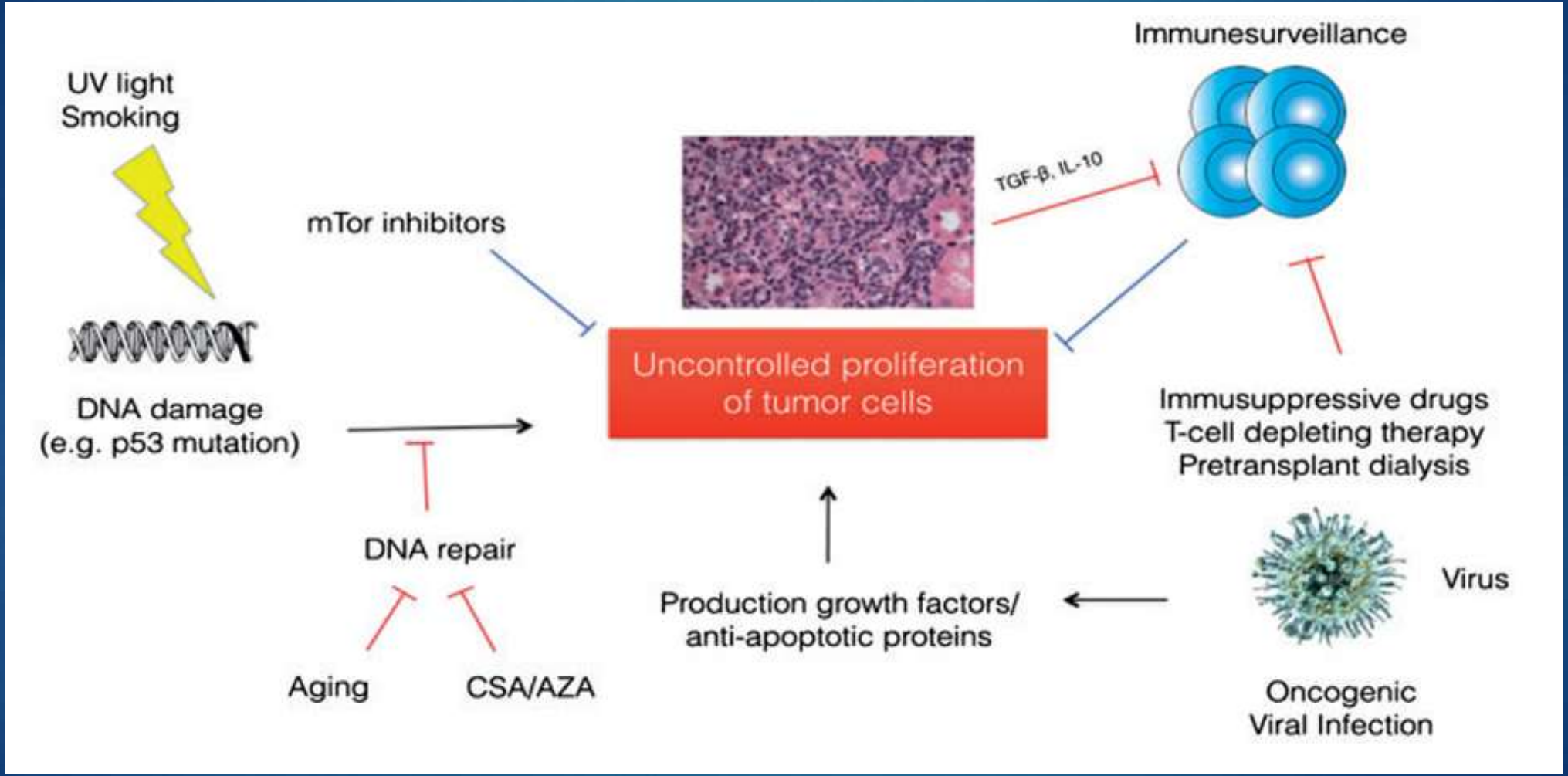
- 1.Introduction
- 2.Pathogenesis
- 3.Epidemiology
- 4.Risk factors
- 5.Common malignancy after renal transplantation
- 6.Screening and Surveillance
- 7.Waiting time prior to renal transplantation
- 8.Management principles
- 9.Graft and patients outcomes and prognosis
- 10.Conclusion

1.Introduction and Objective

- Burden of malignancy after kidney transplantation
- Malignancy is the leading cause of death in kidney transplant recipients
- Responsible for **15-30 %** of late post transplant mortality
- Increased cancer risk vs general population **(2-4 times higher cancer risk)**
- Impact on graft survival and patient mortality
- Role of chronic immunosuppression
- Impaired immune surveillance
- Oncogenic viruses(EBV,HPV,HBV,HCV,HHV-8)
- Drug specific effects(CNIs, azathioprine ,mTOR inhibitors)
- Skin cancers , PTLD, and virus associated tumors predominate

2.Pathogenesis

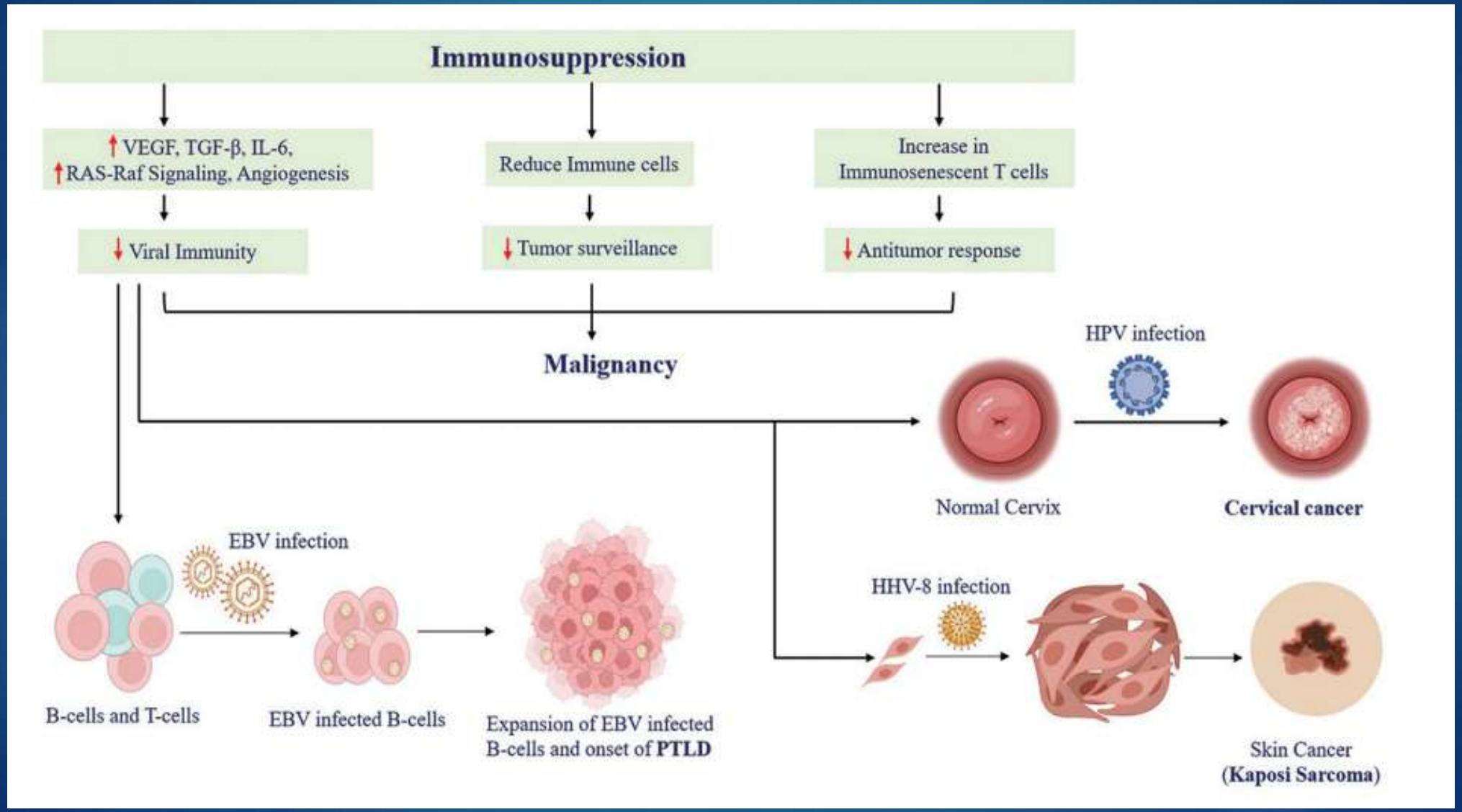
2.Pathogenesis:
Carcinogenesis post kidney transplantation



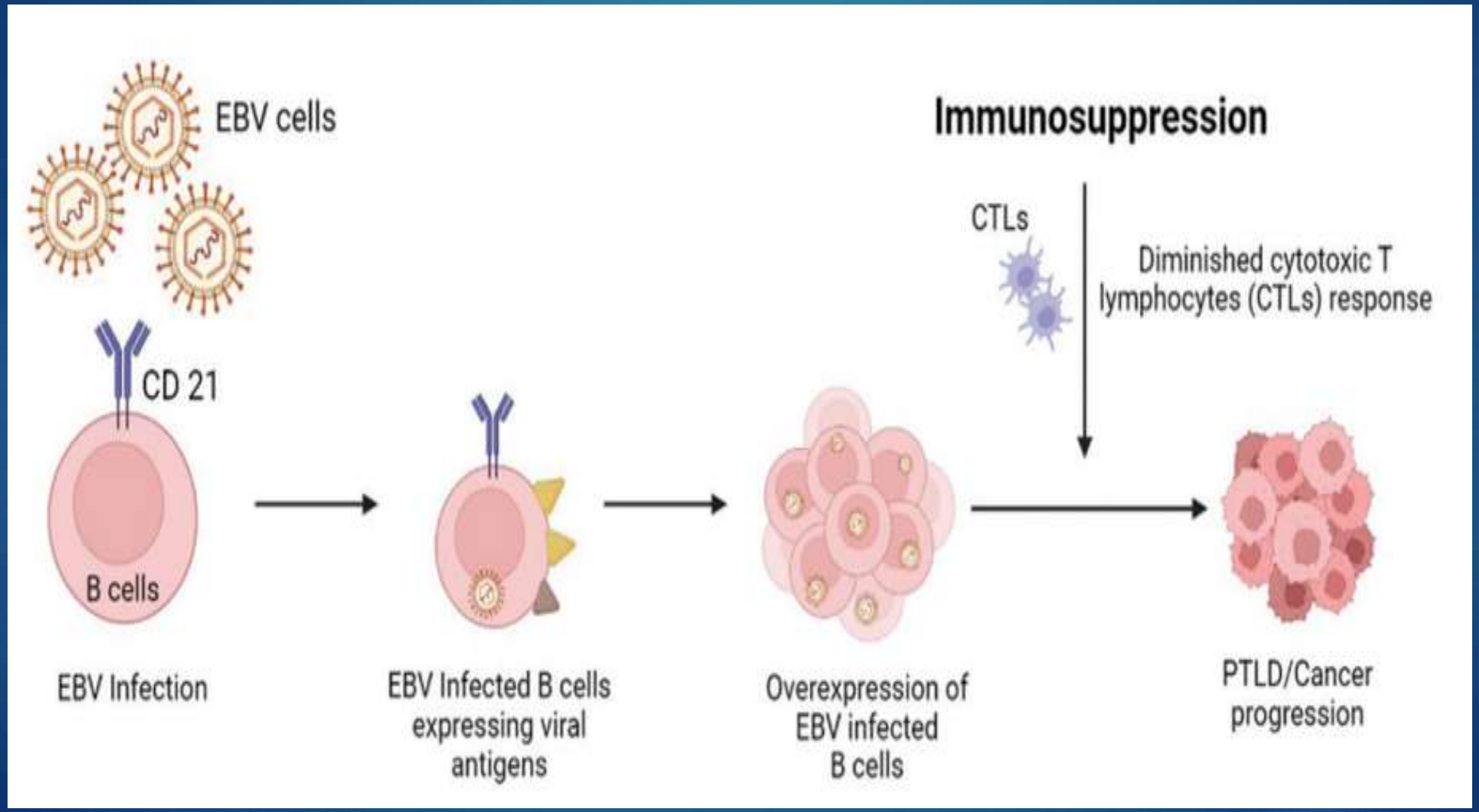
Riellla LV.Mailgnancy after kidney transoplantation

Sprangers etal Clinical Kidney Journal ,2018,vol.11,no,3,315-329

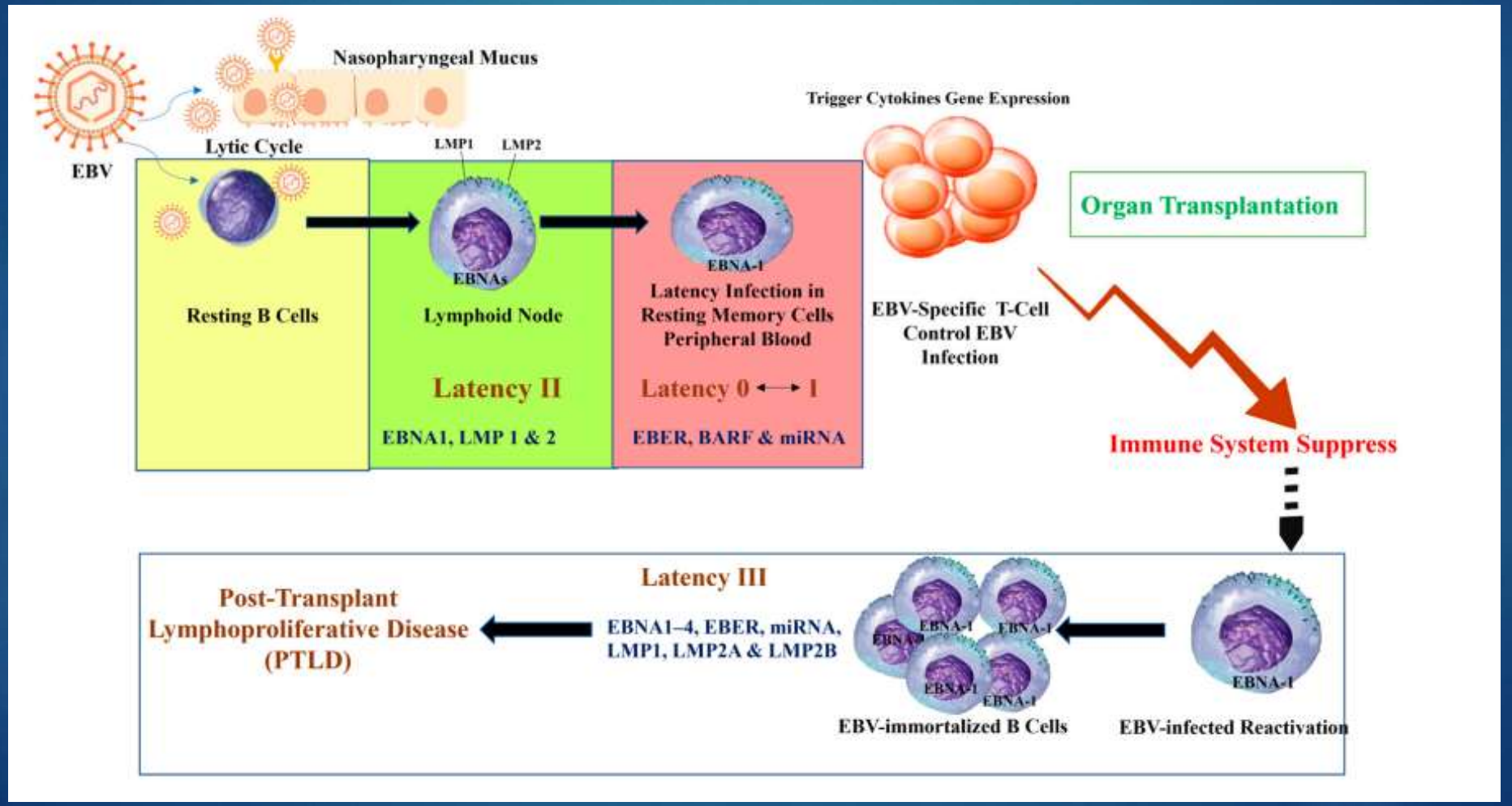
Pathogenesis of virus-induced posttransplant malignancy.



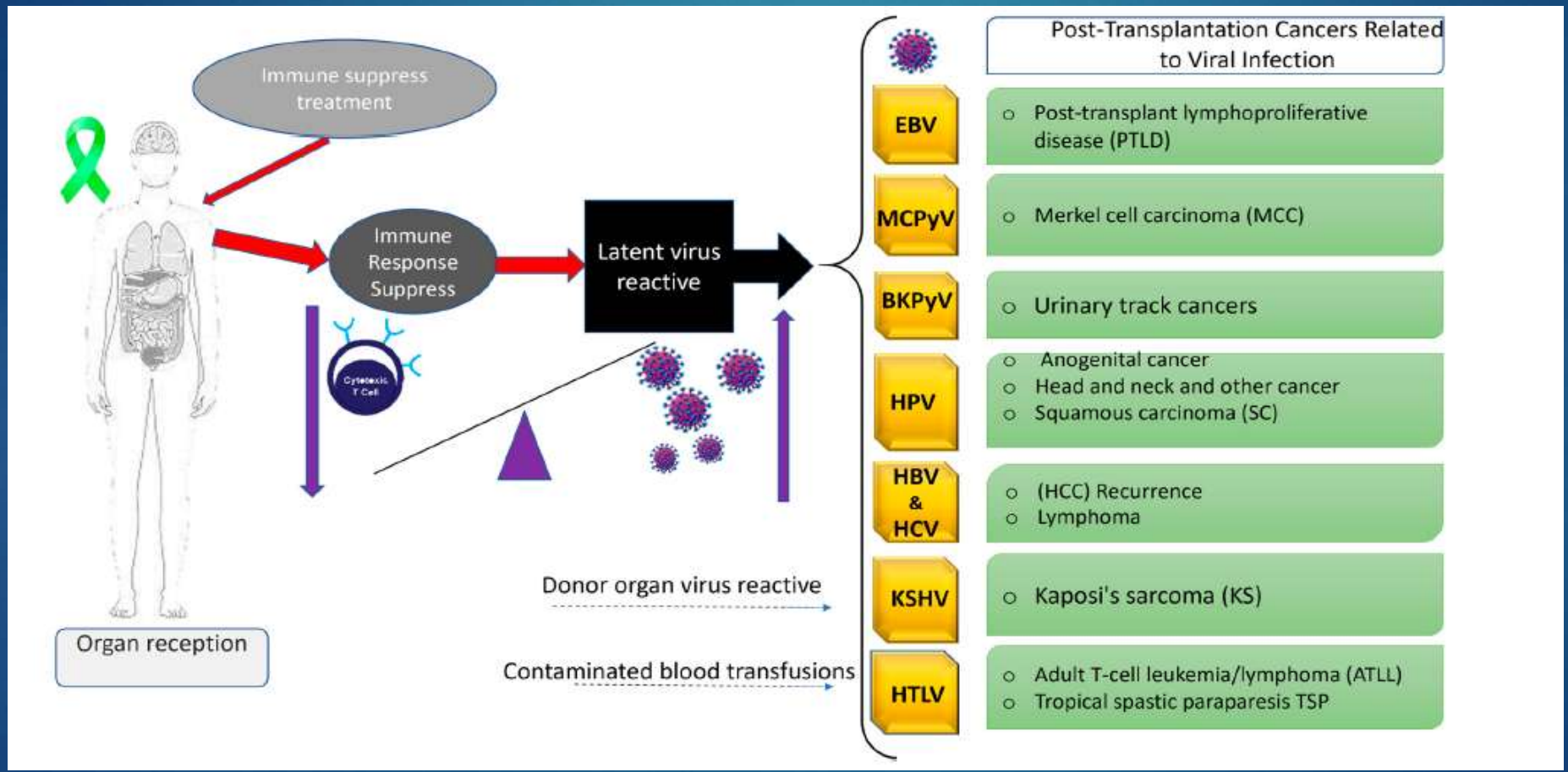
Pathogenesis of posttransplant lymphoproliferative disease in kidney transplant recipients.



Latent EBV in transplant recipients causes **PTLD** through long-term persistence. EBV can persist in B cells in different latency states. Under immunosuppression, such as after organ transplantation, EBV can reactivate, leading to uncontrolled B-cell proliferation and the development of PTLD.



Oncogenic Viruses



3. Epidemiology

Epidemiology of post renal transplant malignancy

- **1.Overall Risk**

  2-4 fold increased overall cancer risk compared with the general population

- **2.Lifetime risk**

  10-25 % of kidney transplant recipients develop at least one malignancy during long term follow up

- **3.Incidence rate**

  2-3 % per year ,cumulative risk increased with time

Time after transplant	Risk
1 year	2-3 %
5 years	10-15 %
10 years	20-30 %
20 years	Up to 40-50 %

Epidemiology of post renal transplant malignancy

- Time distribution after transplant
-

Time period	Common malignancy
Early (< 1 year)	PTLD, donor- derived tumors
Intermediate (1-5 yrs)	PTLD, virus – related cancers
Late (> 5 yrs)	Solid organ tumors

Epidemiology of post renal transplant malignancy

- **Geographic Variations**
- **Middle east and Australia:**

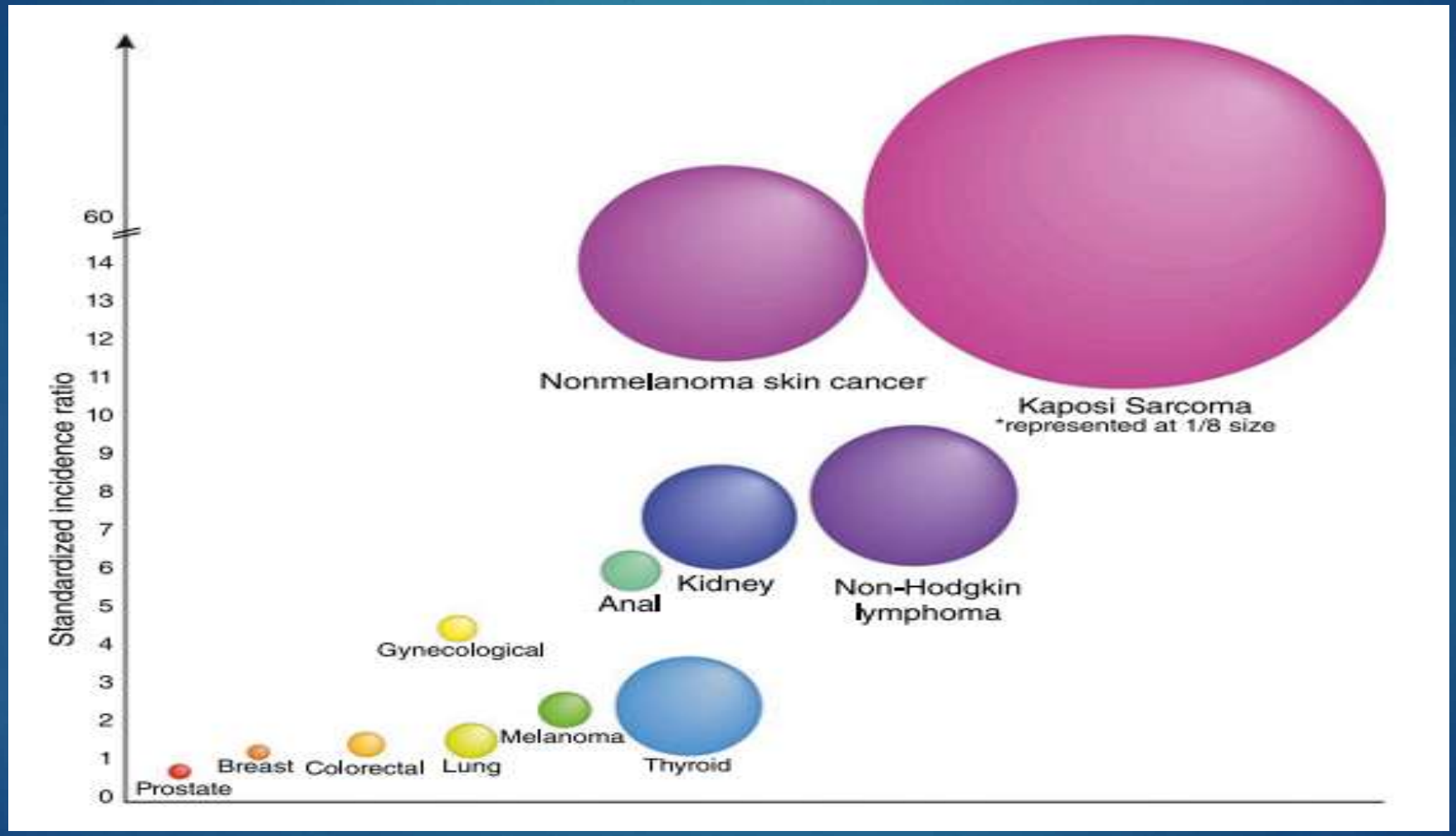
  High UV exposure regions

  Extremely high skin cancer rates
- **Mediterranean and middle east:**

  High Kaposi Sarcoma
- **Asia:**

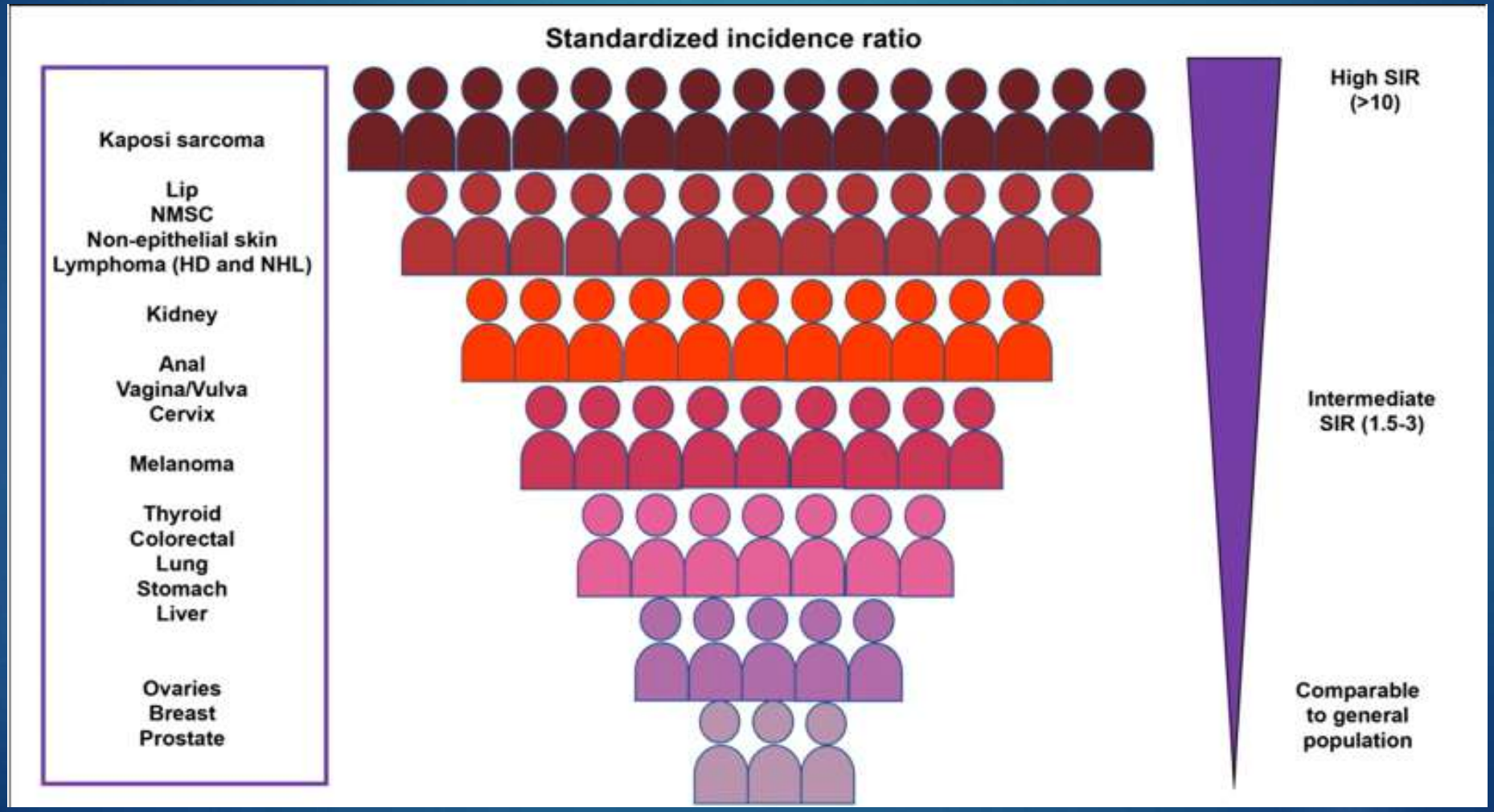
  Higher virus –related malignancies (EBV,HBV,HPV)

Incidence of All-Cause and Site-Specific Cancer after Transplantation



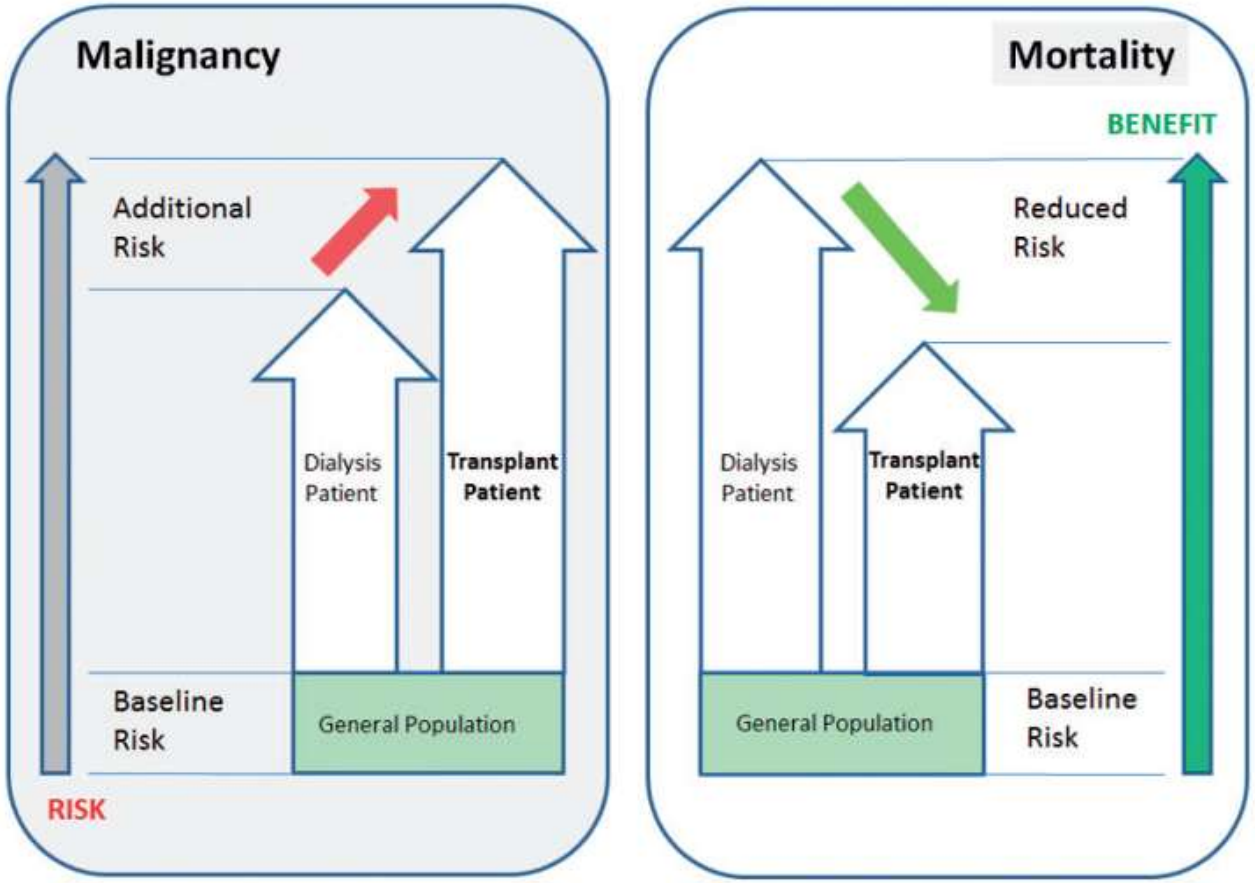
David Al-Adra,1 Talal Al-Qaoud etal:CJASN:17(3):434-443, March 2022.

Standardized Incidence Ratio (SIR)



4.Risk factors

Risks for malignancy and mortality are elevated in dialysis patients



- Older age
- Male gender
- Longer time on dialysis
- Smoking
- Sunlight exposure
- Prior malignancy
- Increased total immunosuppression
- Azathioprine
- T-cell-depleting antibodies

Factors contributing to increased rates of malignancies after kidney transplantation

Malignancy risk in KT recipients exposed to IS pre Tx for the treatment of GN

Malignancy risk in kidney transplant recipients exposed to immunosuppression pre-transplant for the treatment of glomerulonephritis

Background

Pre-transplant immunosuppression (PTI) for the treatment of glomerulonephritis (GN) may contribute to an individual's cumulative immunosuppression burden, and may impact the development of malignancy in post-kidney transplant.

Methods

Single center study
University of North Carolina-Chapel Hill

- Kidney transplant recipients from 2005–2020
- Pre-transplant PTI (n=184)
- Control: transplant recipients never exposed to PTI (n=579)

PTI: Cyclophosphamide (CYC), Rituximab (RTX), Mycophenolate (MMF), Calcineurin inhibitor (CNI)

Outcomes: solid or hematologic malignancy, non-melanoma skin cancer (NMSC), PTLD

Results

	Malignancy	NMSC	PTLD
Control	Ref	Ref	Ref
GN PTI	aHR1.82 (1.10–3.00)	aHR1.09 (0.64–1.83)	aHR1.02 (0.40–2.61)

Type of PTI	Malignancy (vs. control)
CYC	HR 2.59 (1.48–4.55)
RTX	HR 3.82 (1.69–8.65)
MMF, CNI	NS

Conclusion

Use of PTI, particularly CYC and even RTX, for the treatment of GN is associated with an increased risk for developing malignancy post-transplant.

ERA ndt NEPHROLOGY DIALYSIS TRANSPLANTATION

Massicotte-Azarniouch, D., et al. NDT (2022)
@NDTSocial

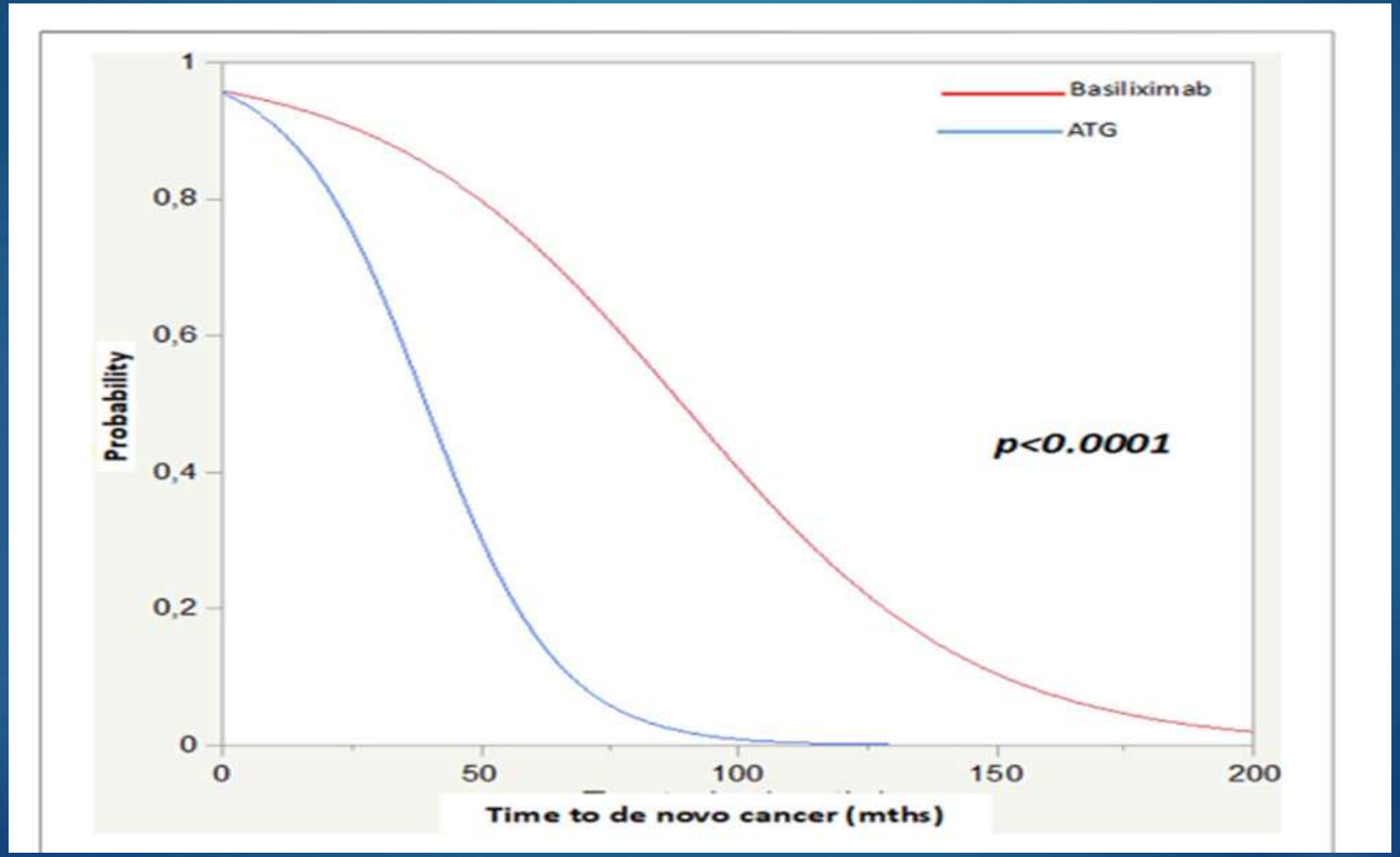
5.Risk factors associated with post–kidney transplant malignancies

B.Sprangers etal. 2017 an article from the Cancer-Kidney International Network

Patient-related risk factors	Recipient age
	Previous cancer
	Sun exposure
	Viral infection
	Duration of dialysis
Transplant-related risk factors	Donor transmission
	Donor type
	Rejection
Medication-related risk factors	Net immunosuppression
	Induction therapy
	Maintenance therapy

Competing risk analysis: Basiliximab and ATG in relation to time to cancer diagnosis post-Kidney transplantation

Re Sartò GV, etal (2024) Post-Kidney Transplant Cancer: A Real-Worldretrospective Analysis From a Single Italian CRenter. Transpl Int 37:13220.



Immunosuppressive drugs and oncogenesis

Immunosuppressant agent	Method of action	Role in carcinogenesis
Calcineurin inhibitor	Inhibition of IL-2 production through binding and inhibition of cyclophilin (cyclosporine) and FKBP-12 (tacrolimus), respectively	Production of TGF-β [98, 99] Production of VEGF [98, 100] Production of interleukin-6 (IL-6) (promotion of EBV-induced B-cell growth) [101] Promotion of invasive behaviour of non-transformed cells [98] Reduced ability to repair radiation-induced DNA damage Enhanced apoptotic effects of taxol and IFN-γ on human gastric and bladder cancer cells [102, 103] Increased rate of lymfoproliferative disorders in HSV-infected mice [104]
Azathiopurine	Inhibition of DNA and RNA synthesis through incorporation of thiopurine analogues	Intercalation at the DNA level, inhibiting repair splicing and eliciting codon misreads [105] Increased development of microsatellite DNA instability [106]
Mycophenolate mofetil	Inhibition of inosine monophosphate dehydrogenase and *de novo* purine biosynthesis	Anti-proliferative effect on leukaemia and solid tumour Inhibition of adhesion molecules [107, 108–114] Suppressed glycosylation and expression of several adhesion molecules [109, 115] Inhibition of adhesion of colon adenocarcinoma cells to endothelial cells [116]
mTOR inhibitors	Inhibition of mTOR pathway	Direct antitumour effect by inhibition of mTOR pathway [117, 118] Inhibition of angiogenesis Inhibition of p70 S6K: decreasing cancer cell proliferation [119, 120 Inhibition of interleukin-10: decreasing tumour cell JAK/STATs activity [120] Inhibition of cyclins: blocking cell-cycle activity [121] Decreased VEGF-A and VEGF-C signalling: impaired tumour angiogenesis [101, 119, 122, 123] Inhibition of growth signals in PTLD-associated EBV $^{+}$ B-cell lymphomas [124] Inhibition of replication of EBV-positive B cells, T cells and NK cells [125, 126] Inhibition of ultraviolet B–induced metalloproteinase activation [127]

5.Common malignancy after renal transplantation

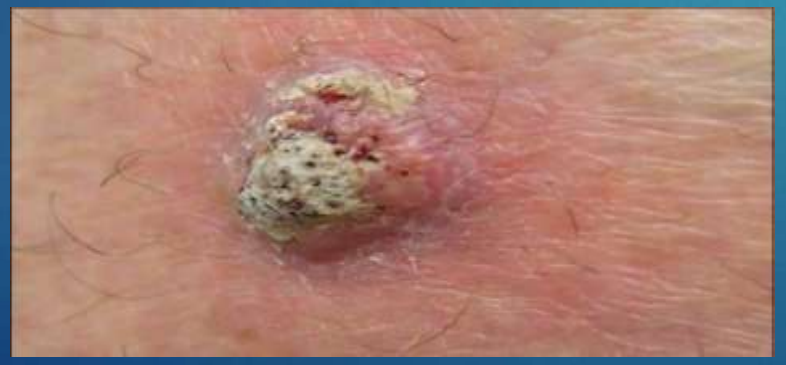
Common malignancy after renal transplantation

- Skin cancers (most common overall **40-50%**)
  - -Squamous cell carcinoma (SCC)
  - - Basal cell carcinoma(BCC)
- Post transplant lymphoproliferative disorder PTLD
- Kaposi Sarcoma
- Solid organ malignancies
  - - Renal cell carcinoma
  - - Colorectal cancer
  - -Lung cancer
  - - Anogenital cancers

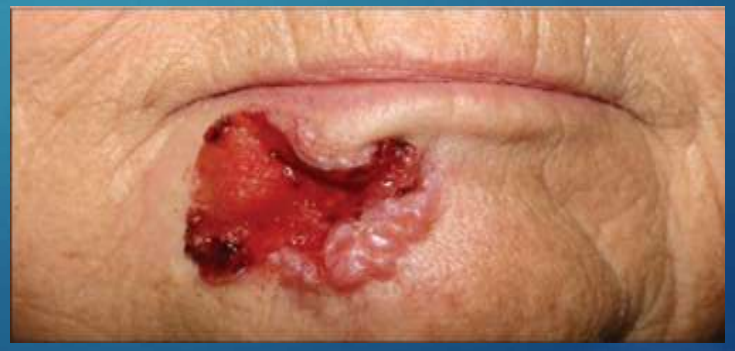
1.Skin cancer-Most common

- Accounts for **40-60 %** of all post transplant cancers
- Non melanoma skin cancer
- Squamous cell carcinoma most common
- Basal cell carcinoma
- More aggressive Behavior
- Higher recurrence and metastasis

Squamous cell carcinoma



Basal cell carcinoma

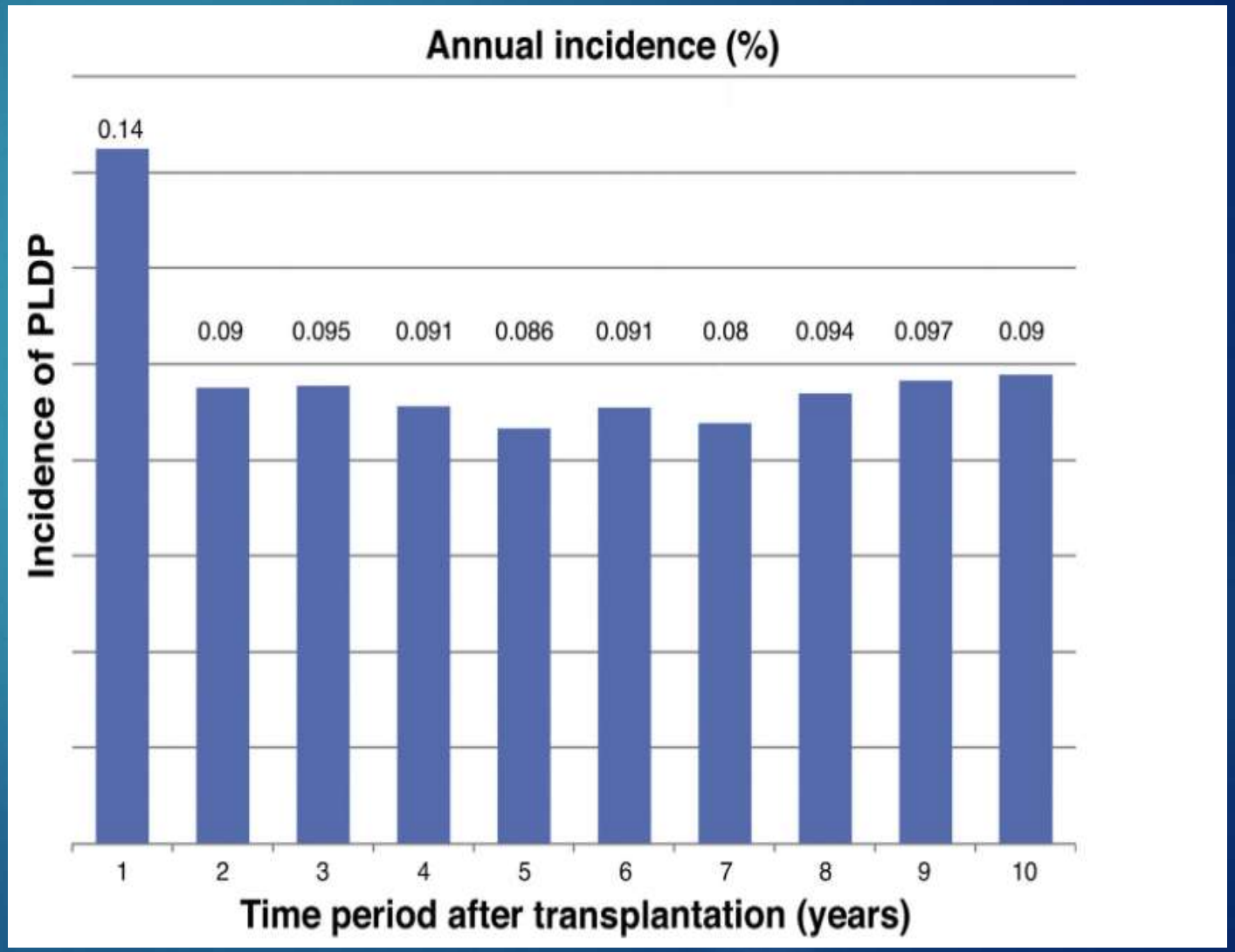


2.PTLD

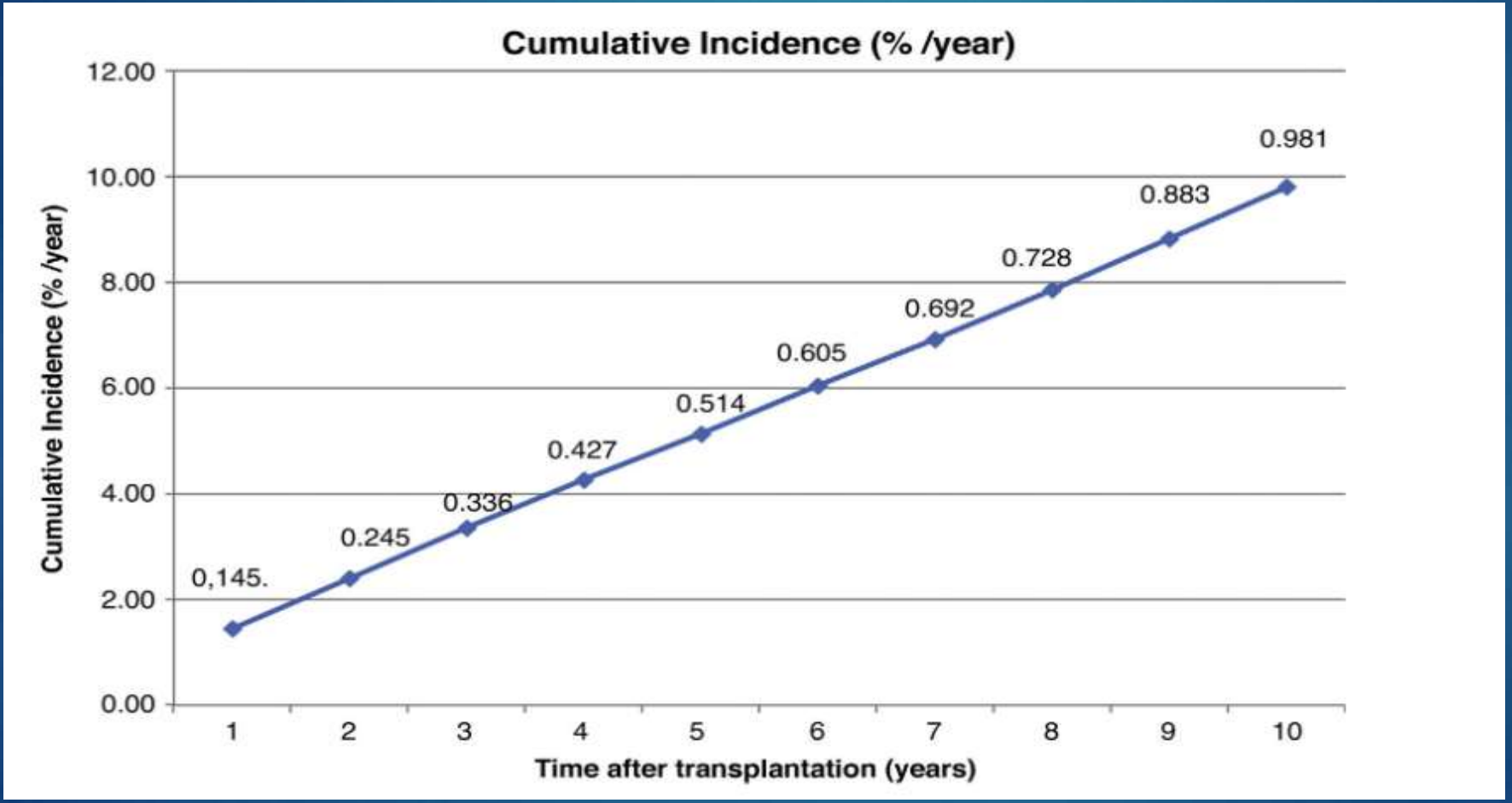
Annual incidence of post-transplant diffuse lymphoproliferative disease in 10 years.

Lymphoproliferative disorders after renal transplantation along 2 decades: a large longitudinal study of 21.546 recipients

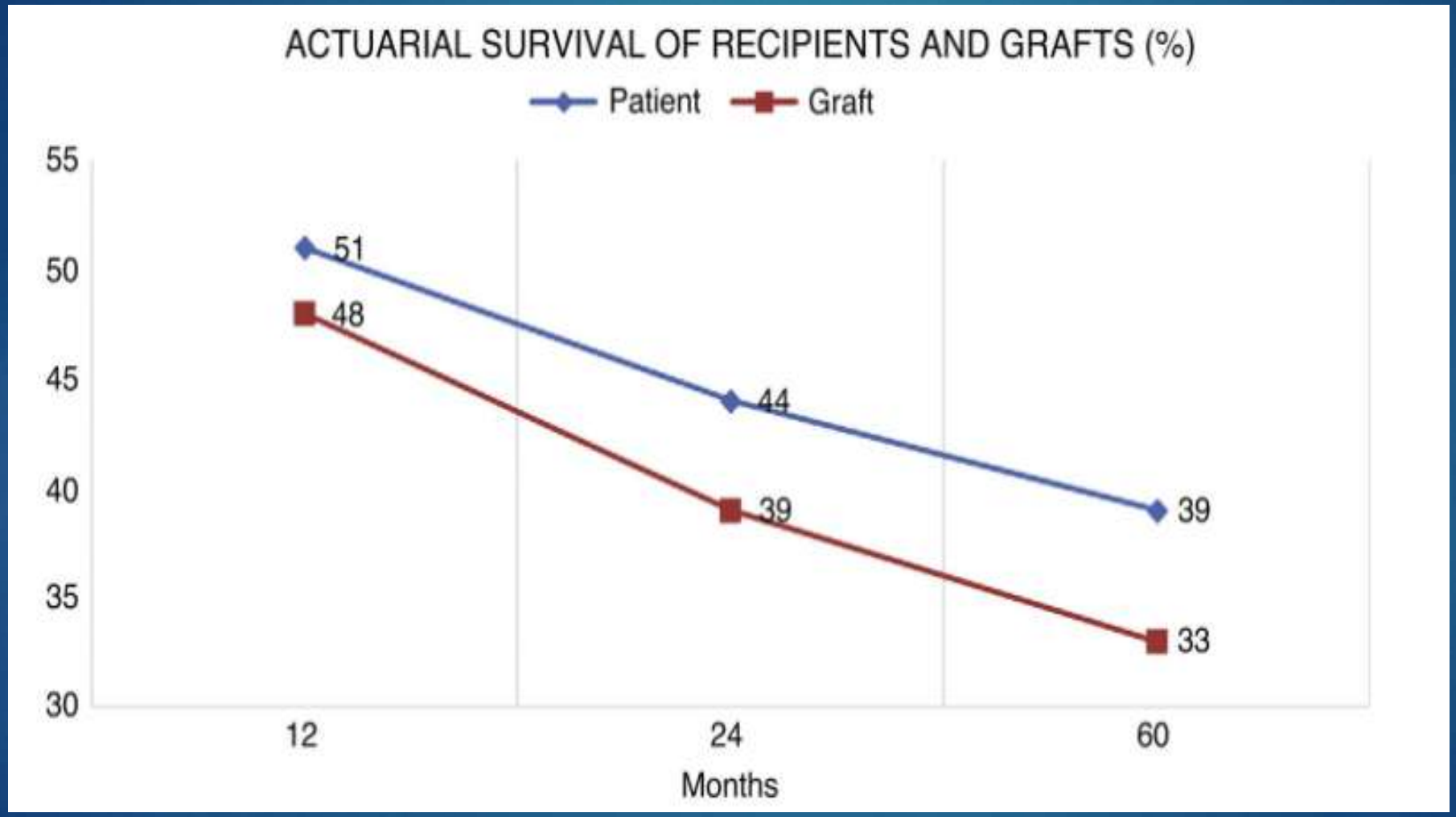
Antonio Franco[a,], Domingo Hernandez[b], Sofia Zarraga[c], Ana Sanchez Fructuoso[d], Marta Crespo[e], Auxiliadora Mazuecos[f], Carmen Diaz Corte[g], Alberto Rodriguez Benot[h], Juan Carlos Ruiz[i], Isabel Beneyto[j], en representación del grupo GREAT*



Annual incidence of post-transplant diffuse lymphoproliferative disease in 10 years.



Patient and graft survival after diagnosis of lymphoproliferative disease.



How I Treat Post-Transplant Lymphoproliferative Disorder (PTLD)

Diagnostic Considerations

Pathological review for PTLD subtype:
- Non-destructive, Polymorphic, Monomorphic, Hodgkin-like

EBV status

Frontline Setting

Reduce immunosuppression
If CD20 + Rituximab monotherapy
Sequential chemoimmunotherapy in non-responders or high-risk disease

Relapsed PTLD

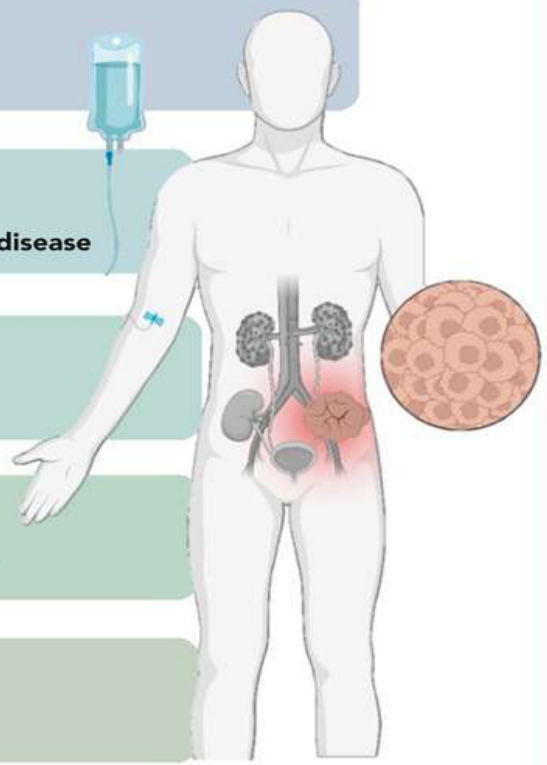
Re-challenge with rituximab
EBV(+): Brentuximab vedotin (BV) if CD30+; EBV CTLs
EBV(–): HSCT; CAR T

Rare Subtypes

Hodgkin Lymphoma: Hodgkin-like treatments
Primary CNS-PTLD: HD-MTX-Rituximab
Plasmablastoid: Consider BV if CD30+; Daratumumab if CD138+

Precautions

Organ rejection, dysfunction
Drug-drug interactions
Cytopenias and infections



Conclusions:

1) PTLD is a potentially life-threatening complication of solid organ transplant
2) Adoptive immunotherapies represent a promising option for relapsed disease

*Amengual and Pro. DOI: 10.1182/**blood**.2023020075*

***Blood* Visual Abstract**

3.Kaposi Sarcoma

Kaposi Sarcoma

BACKGROUND

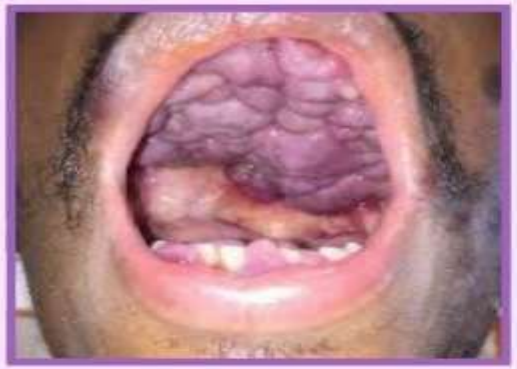
- Indolent angio-proliferative spindle-cell tumor derived from endothelial and immune cells
- infected with human herpes virus type 8 (HHV-8; also known as Kaposi sarcoma herpes virus

CLINICAL PICTURE

- Macular, papular, nodular, or plaquelike appearances
- Lesions may assume a brown, pink, red, or violaceous color
- Odynophagia, dysphagia
- Nausea, Vomiting, abdominal pain
- Hematemesis, hematochezia, melena
- Bowel obstruction

INVESTIGATION

- Tests to diagnose internal Kaposi's sarcoma include: Fecal occult blood test.
- Biopsy done for it



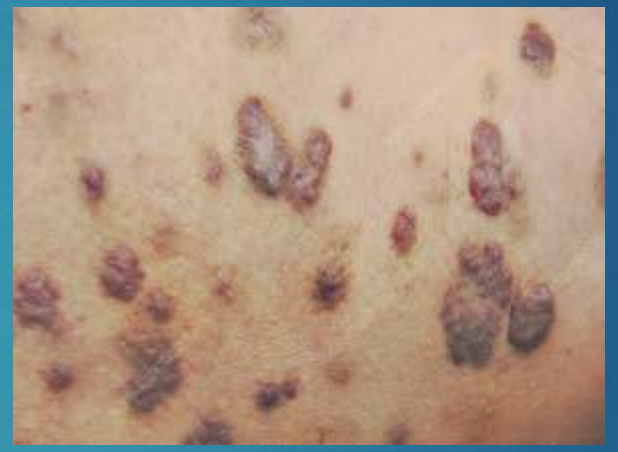
TREATMENT

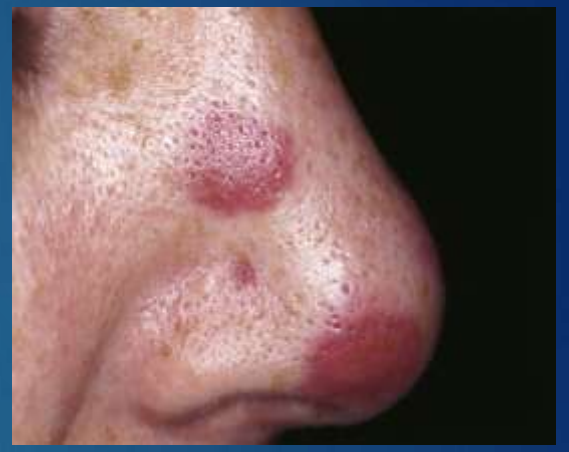
- Currently, no treatment is available to eradicate HHV-8 infection
- Therapy for epidemic Kaposi sarcoma centers on the use of highly active antiretroviral therapy (HAART)

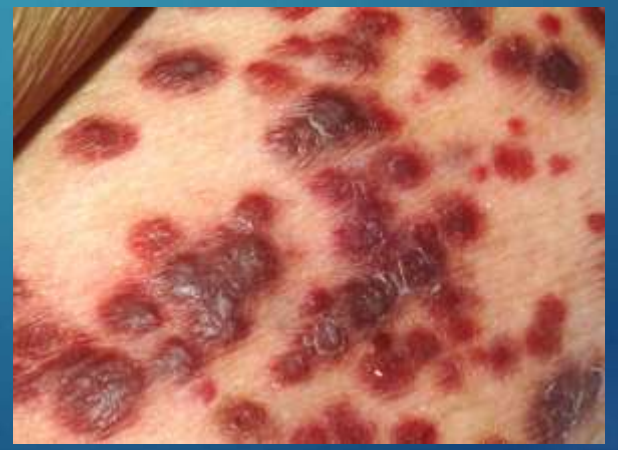
- Affecting up to 5% of transplant patients
- Incidance:100 times in ethnic groups as compared to the general population

Post-transplant virus associated malignancy and their diagnosis

Post-transplant viral associated malignancy	Diagnosis
PT-KS	Examine for cutaneous or mucosal lesions, visceral involvement and haematological manifestations Diagnostic gold standard: HHV8 confirmation in biopsy of KS lesions[170] HPE characteristic of PT-KS: Spindle-shaped cells and immunostaining confirmation with latency-associated nuclear antigen and CD34 positive staining[171,172] Quantitative PCR load of HHV8: Role in supporting diagnosis and monitoring treatment response Confirmation of diagnosis by HPE and HHV8 DNAemia Depending on site involved, disease staging by imaging and invasive procedures (*e.g.*, bronchoscopy, esophago-gastroduodenoscopy, colonoscopy)[173]

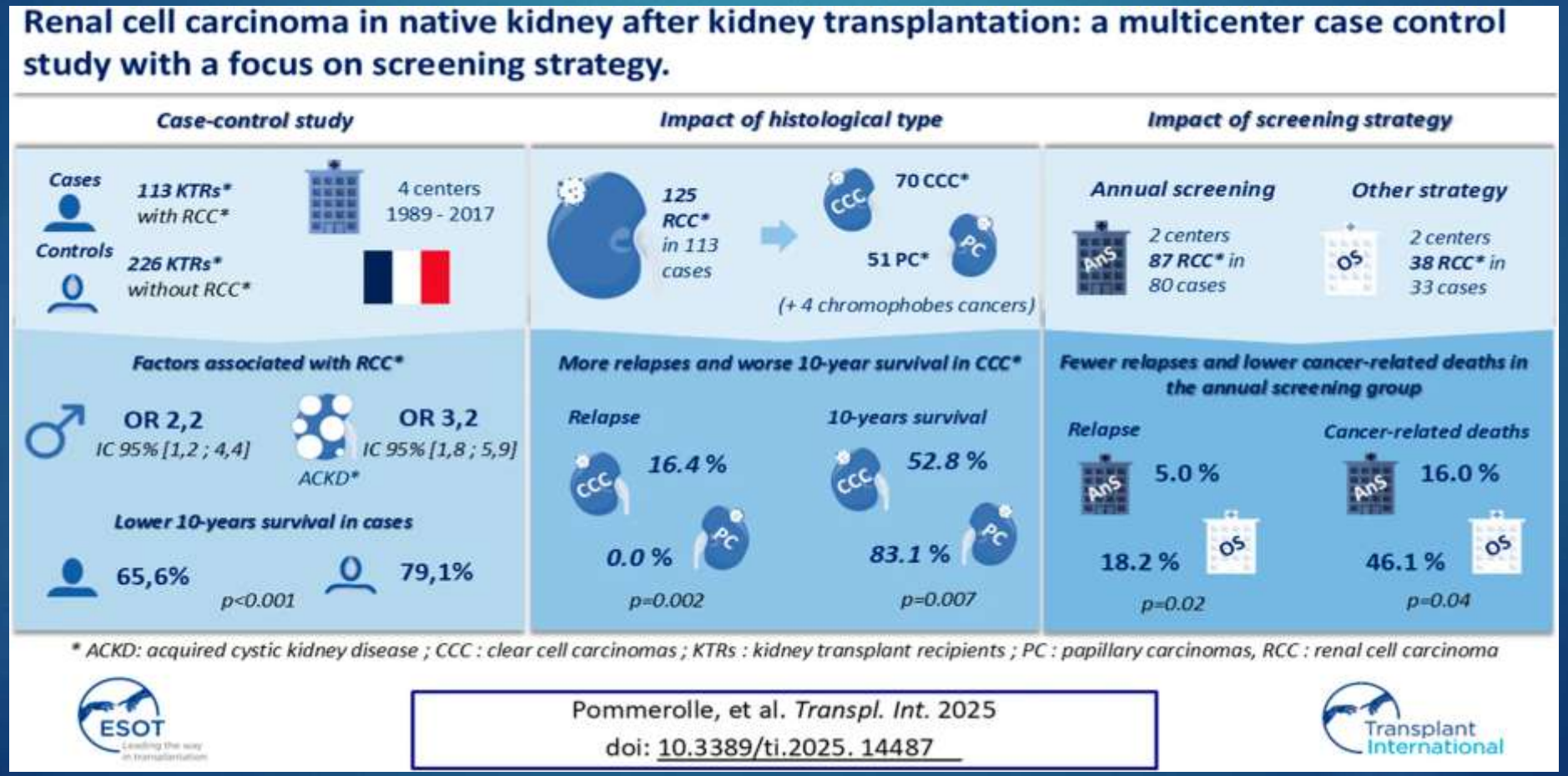






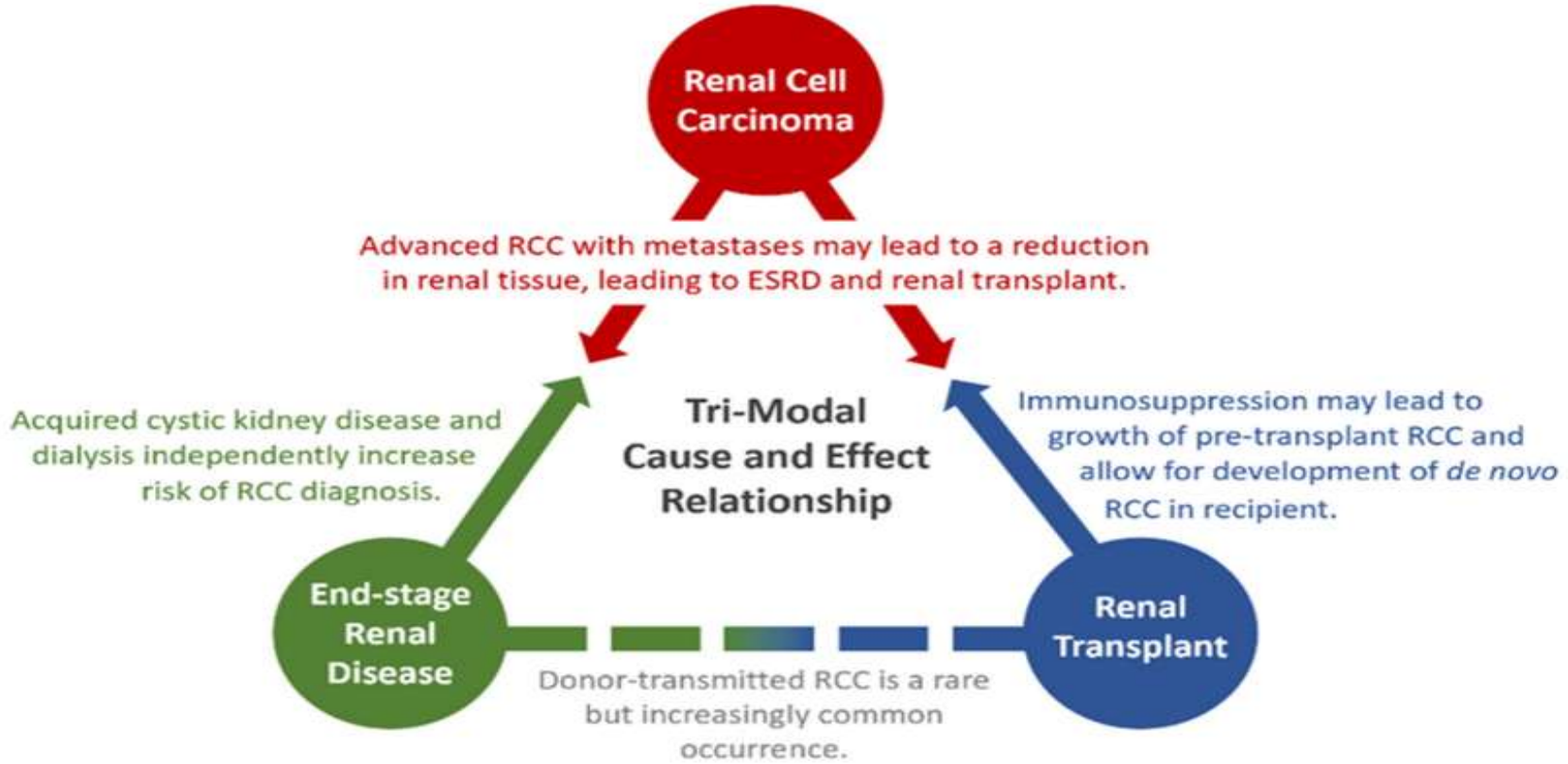
4.Renal cell carcinoma

- Discovered in **3.4%–3.9%** of individuals who undergo screening for asymptomatic renal transplant candidates.
- Long-term dialysis use, obstructive, uropathy, toxic, or infectious etiologies for renal disease and acquired cystic kidney disease



Triangular cause and effect diagram, visualizing the bidirectional relationships between RCC, ESKD, and transplantation.

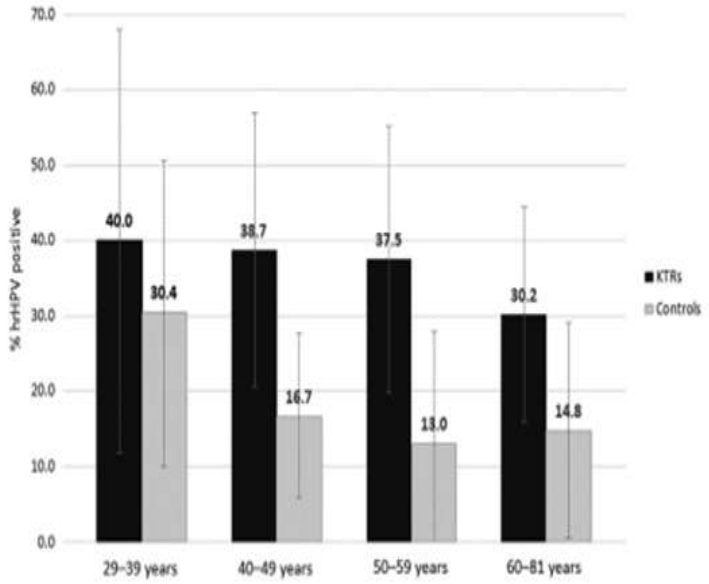
Robinson, S.;etal RCC and the Role of Transplantation. Cancers 2024, 16, 3. https://doi.org/10.3390/cancers16010003



5.Cervical and anogenital cancers

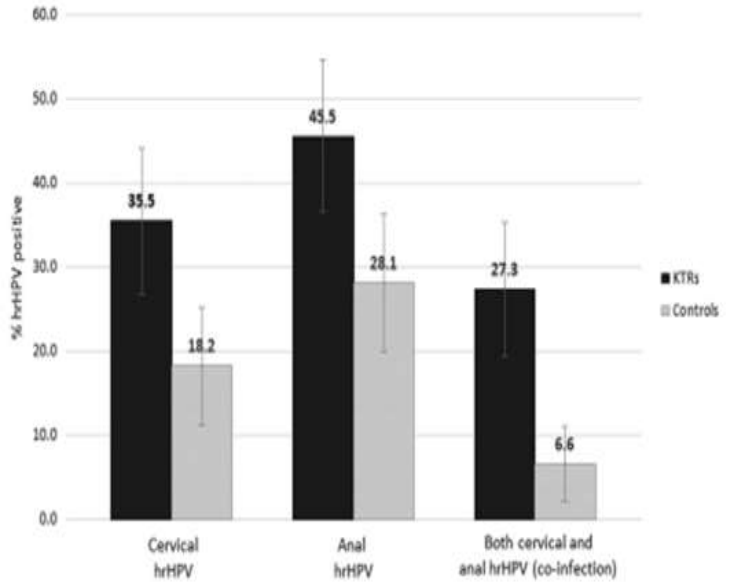
1.Age-specific prevalence of cervical hrHPV infection in (KTRs)
2.Prevalence of cervical and anal hrHPV co-infection in (KTRs)

Prevalence of cervical human papillomavirus and the risk of anal co-infection in kidney transplant recipients: Results from a Danish clinical study



Transplant Infectious Dis, Volume: 25, Issue: 2, First published: 25 January 2023, DOI: (10.1111/tid.14019)

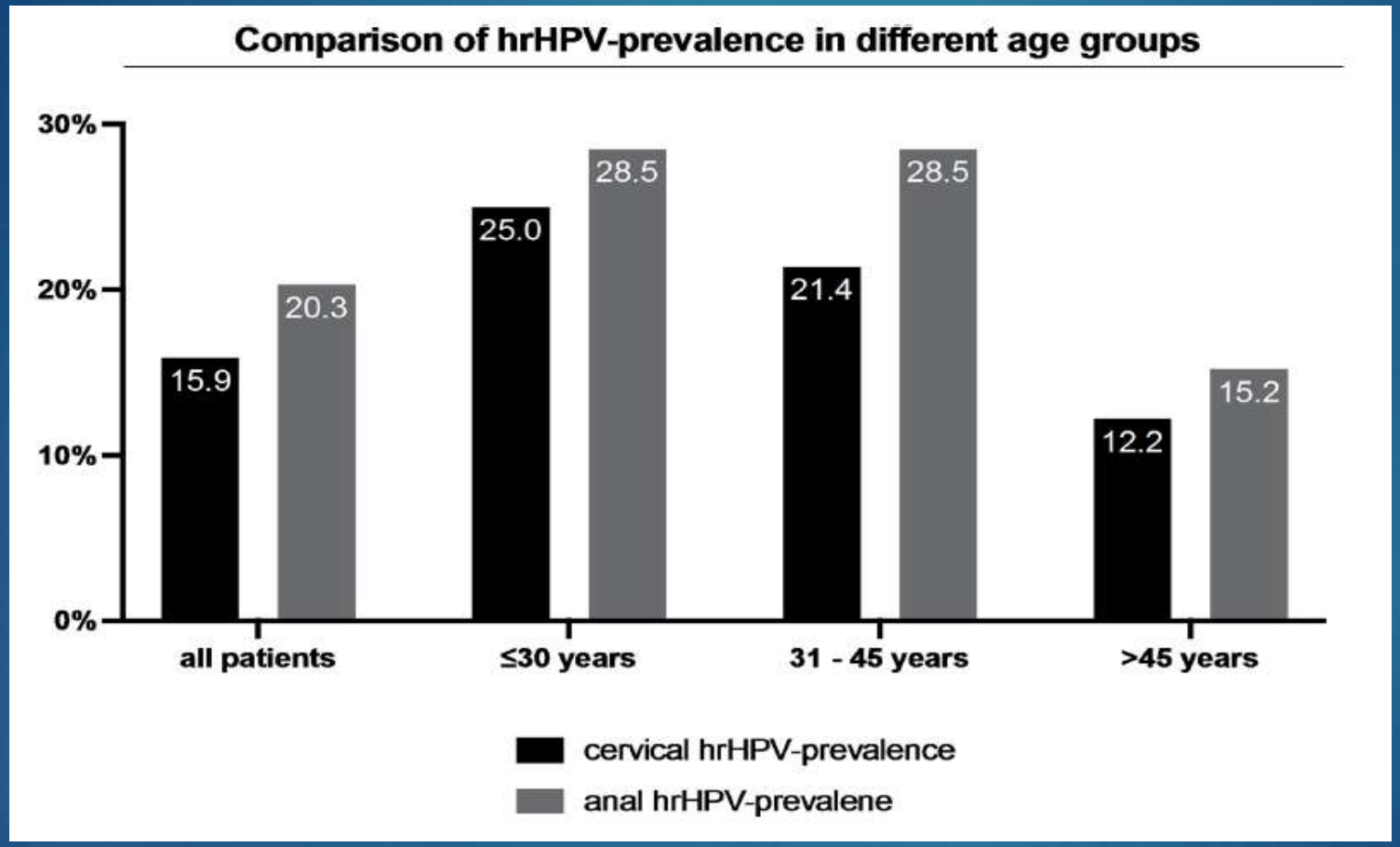
Prevalence of cervical human papillomavirus and the risk of anal co-infection in kidney transplant recipients: Results from a Danish clinical study



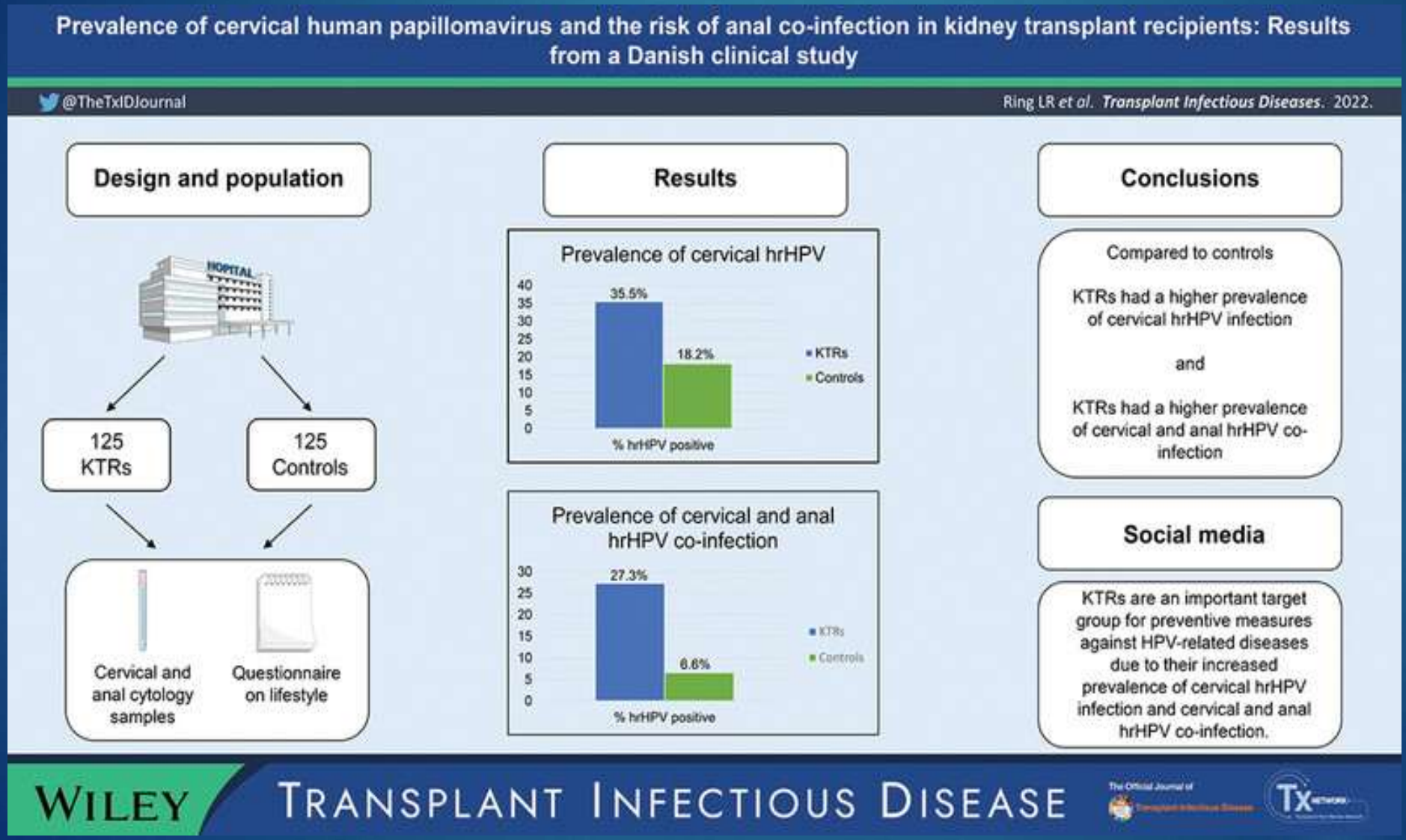
Transplant Infectious Dis, Volume: 25, Issue: 2, First published: 25 January 2023, DOI: (10.1111/tid.14019)

Comparison of hrHPV prevalence in different age groups

Hillen et al. BMC Women's Health (2025) 25:290 https://doi.org/10.1186/s12905-025-03813-0

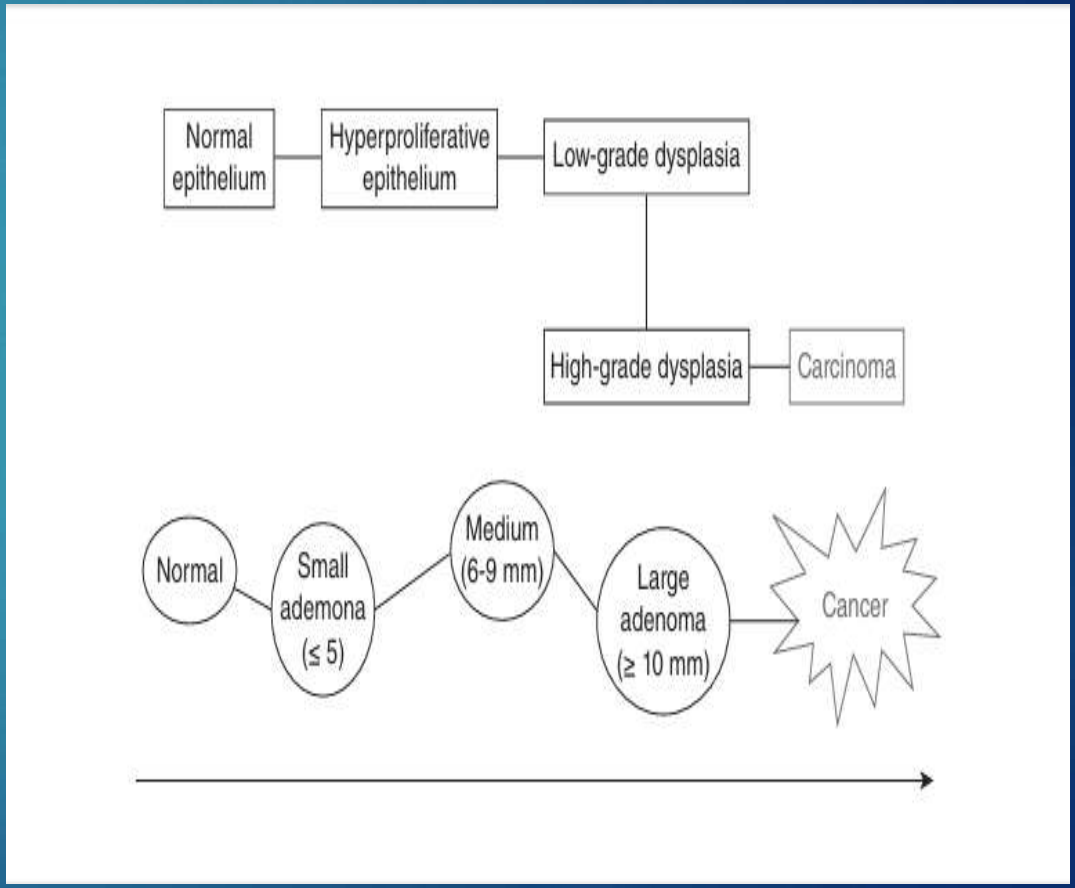


Cervical and anogenital cancers



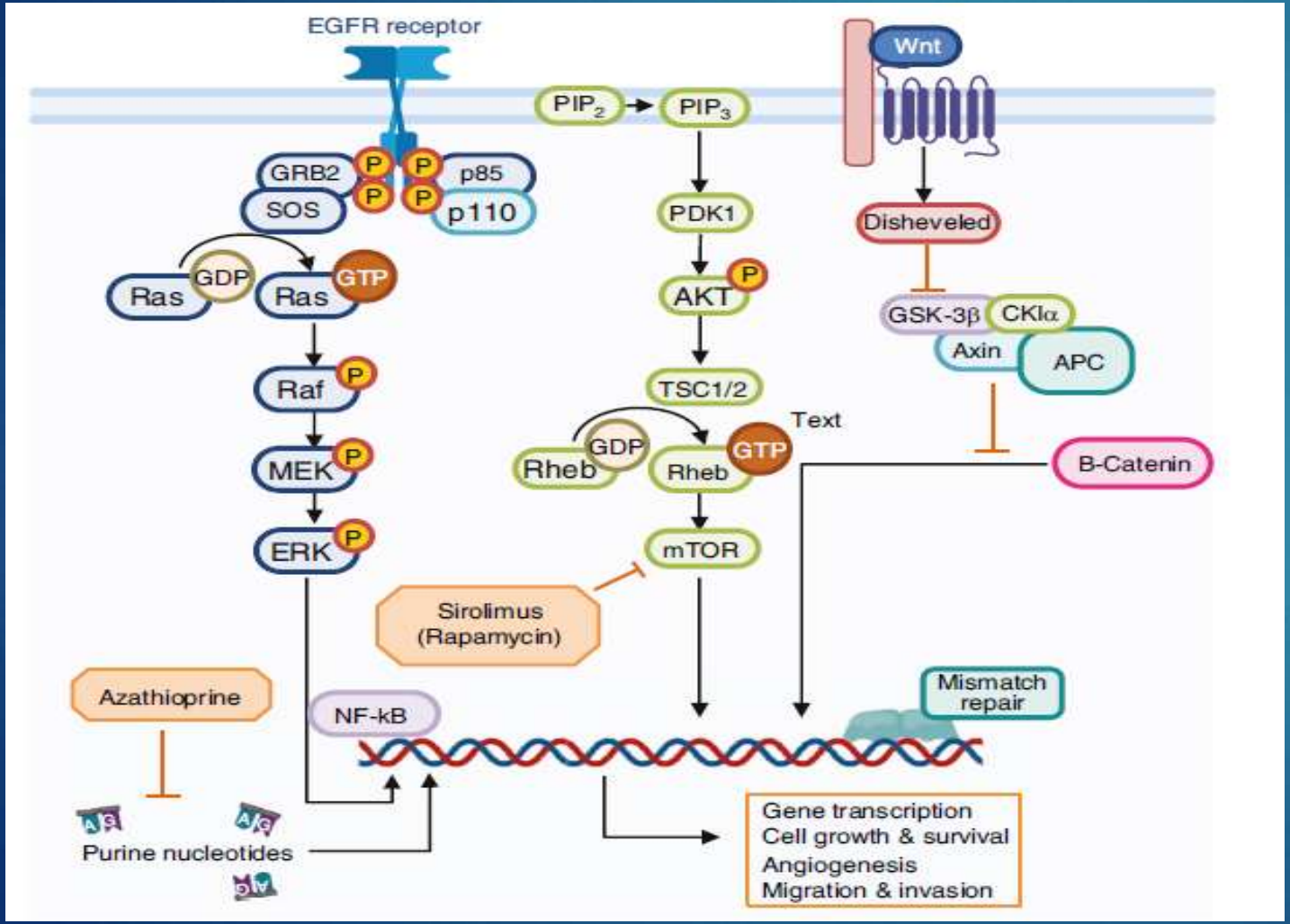
6.Colorectal cancer

- **Increased risk** (≈2–3× general population)
- Risk increases with age and time post-transplant
- **Mechanism:** immunosuppression, oncogenic viruses, drug effects
- Often presents at advanced stage
- **Colonoscopy preferred;** consider earlier screening
- **Management:** surgery ± chemotherapy + IS modification



Main intracellular pathways within intestinal epithelial cells that may lead to de novo CRC in KT patients

British Journal of Cancer; https://doi.org/10.1038/s41416-025-02994-7



- 1)chromosomal instability (e.g., APC)
- 2) mutations in DNA mismatch repair (e.g., MLH1, MLH2)
- 3) inappropriate activation of proto-oncogenes (e.g., Ras), and deregulation of the phosphatidylinositol-3-kinase (PI3K) pathway
- [4]. Inhibitors of mTOR and purine nucleotide synthesis may have anti-oncogenic properties.

Colorectal cancer

Author (Year)	Country	Study Design	Sample Size and Characteristics	Immunosuppressive Regimens and Dosages	Key Findings
Pendon-Ruiz de Mier et al. (2015) [41]	Spain	Retrospective cohort (1979–2015)	1450 KTRs; 90 developed PTMs; mean age at transplantation 59 years (with cancer), 53 years (without cancer)	Triple therapy with CNIs, mycophenolate/azathioprine, and prednisolone. Induction with basiliximab or thymoglobulin	CRC in 11% of SOC (≈10/90 cases) CRC ~0.7% prevalence (3/194); survival after SOC diagnosis ~2 years
Piselli et al. (2023) [42]	Italy	Cohort (1997–2021)	11,418 KTRs (63.8% male, 36.2% female); median age at transplantation 50 years; 1646 PTMSs	1997–2004: predominantly cyclosporine 2005–2012: predominantly tacrolimus 2013–2021: predominant combinations including mTORi	CRC incidence: 0.4 per 1000 person-years in 1997–2004 (7 cases), 0.8 per 1000 person-years in 2005–2012 (29 cases), and 2013–2021 (23 cases). Adjusted IRRs = 1.54; 95% CI: 0.67–3.54 for 2005–2012 and IRR = 1.39; 95% CI: 0.59–3.29 for 2013–2021. SIR = 0.76; 95% CI: 0.58–0.99
Privitera et al. (2021) [43]	Italy	Cross-sectional (matched case–control)	160 KTRs vs. 594 controls; median colonoscopy after 6.4 years post-transplant	Tacrolimus, mycophenolate, steroids, cyclosporine, and everolimus. Three-drug regimens, with or without induction therapy	22/160 (13.7%) with advanced colorectal neoplasia, 4/160 (2.5%) with CRC; no increased CRC risk vs. controls (OR = 0.69); higher advanced adenoma risk (OR = 1.65)
Pyrza et al. (2022) [44]	Poland	Cross-sectional	350 KTRs; mean age 48 years; malignancies in 70 patients (20%)	CNIs, azathioprine, prednisone	CRC in 3 cases (0.86%); skin and PTLDs most common; limited CRC-specific data
Rosales et al. (2020) [45]	Australia and New Zealand	Retrospective cohort (1980–2016)	17,628 KTRs (61% male, 39% female); median age at transplantation 45 years; 1061 cancer deaths	CNIs, mTORi	Not mentioned

7.Lung cancer

- Transplant patients are likely to be diagnosed at advanced stages of lung cancer.
- Squamous cell carcinoma is more commonly diagnosed in transplant recipients.
- Overall survival after lung cancer diagnosis is worse in transplant patients.

- Incidence of lung cancer in transplant recipients in different countries

Country	Our cohort	Turkey	China	England	Australia	New Zealand
Number of recipients	1 658	4 000	3 462	25 104	3 129 083	605 538
Time interval (years)	41	4,5	40	27	11	11
Incidence (%)	0.3	6	0.8	1.4	1.2	1.3

Epidemiology & Prognosis

- **2- 4** fold higher risk of developing lung cancer compared to the general population.
- **LC is the primary cause of cancer-related mortality** in solid organ transplant recipients.
- Patients diagnosed at **Stage III or IV**, the median survival is often **less than 1 year**.
- Most cases **(50–80%)** are diagnosed at advanced stages, typically **5 to 10 years** after the transplant.

Clinical Management in lung cancer

- **The "mTOR Switch":** A pivotal strategy in management is converting patients from calcineurin inhibitors.
- **Graft Protection:** mTOR inhibitors are associated with stabilized kidney function and a slower decline in GFR, offering a dual benefit of cancer control and nephroprotection.
- **Curative Surgery: Radical surgical resection** remains the gold standard for **early-stage (I-II)** disease and is the only path to significantly improved long-term survival in KTRs.

8.Oncogenic Viruses-Associated Post-transplant Malignancies

Epstein-Barr virus (EBV)	Post-transplant lymphoproliferative disorder
Human Herpes virus-8 (HHV-8)	Kaposi's sarcoma
Human Papilloma virus (HPV)	Cervical, anogenital, and nasopharyngeal cancers
Merkel cell polyomavirus	Merkel cell carcinoma of the skin
Hepatitis B and C	Hepatocellular carcinoma
Polyoma BK virus*	Uroepithelial cancers
Human T-cell lymphotropic virus type 1	Non-Hodgkin Lymphoma

Viral infections post-transplant (associated with the potential to develop a malignancy): Screening, diagnosis, and treatment

Post-transplant virus infections	Screening	Diagnosis	Treatment
HPV anogenital/cutaneous manifestation[28,161]	All 9–26-yr: Before transplant, receive 3 doses of HPV vaccine [nine-valent or quadrivalent vaccine (Gardasil 9 or Gardasil; Merck, Whitehouse Station, New Jersey)] or HPV-bivalent vaccine (Cervarix; GlaxoSmithKline, Rixensart, Belgium) in women	Examination and biopsy of atypical lesions	Cutaneous warts: Topicals (patient applied): Salicylic/lactic acid/imiquimod or cryotherapy (provider-applied)
	Males and females (up to age 45 yr): May also be vaccinated with 3 doses of HPV vaccine (nine-valent)	Anogenital, perianal warts/history of receptive anal intercourse warts: colposcopy/anoscopy	Anogenital warts: topicals (patient applied): podofilox/5% imiquimod cream or cryotherapy/TCA /BCA/podophyllin resin (provider-applied)
	Organ recipient's (15–26 yr): Immunize even if they have anogenital warts		Not responding or extensive or resistant warts: refer to dermatologist
	At each visit: bright light skin examination (including feet)		
	Cervical pap smear (with or without HPV PCR co-test): Every 6 mo in first year and then yearly, post-transplant, in females (> 30 yr), irrespective of HPV vaccination status		
	If rejection treated with T cell depleting agents, resume above schedule		
	Follow in all females irrespective of HPV vaccination status		

Viral infections post-transplant (associated with the potential to develop a malignancy): Screening, diagnosis, and treatment

Post-transplant virus infections	Screening	Diagnosis	Treatment
EBV viremia/disease	Identify high risk recipients (*i.e.* EBV D+/R-): EBV viral load once first week, monthly first 3-6 mo, and every 3 mo until the end of the first post-transplant year; Additionally, after treatment of acute rejection[162]	Quantitative EBV load assay [calibrated to World Health Organization IS for EBV DNA) (EBV NAAT)	Reduce immunosuppression with rising EBV loads in EBV-seronegative patients
	EBV disease precedes detectable or rising EBV loads	Whole blood/lymphocyte samples are preferable to plasma (the EBV viral load is greater and becomes detectable sooner), thereby enhancing sensitivity and early detection/reactivation	
	Watch for signs/symptoms: fever, diarrhoea, lymphadenopathy, and allograft dysfunction	Same sample type, assay and laboratory for assessing rise in EBV loads	

Viral infections post-transplant (associated with the potential to develop a malignancy): Screening, diagnosis, and treatment

Post-transplant virus infections	Screening	Diagnosis	Treatment
HHV8 viremia	Post-transplantation, HHV8 serologic testing is not routinely recommended globally	Serological assays (IFA ELISA) which detect HHV8 antibodies against latent and lytic viral antigens (both)[163]. Issues with such assays are inadequate standardisation, variable sensitivity and specificity among tests (60%–100%), and poor agreement with a predefined reference standard. It is still preferable when compared with quantitative PCR in identifying "at risk" transplant patients in endemic regions	RIS if quantitative PCR elevated/rising and/or absent HHV antibodies in "at risk" post-transplant patient or with non-neoplastic KS diseases
	Identify "at risk" before transplant, for HHV8 related disease post-transplant, in endemic zone [*i.e.* R+ (HHV8 reactivation) and D+/R- (HHV8 primary infection)][163,164]	Serological assay which detect HHV8 DNA by quantitative PCR: Its role are: (1) Predicts the occurrence of non-neoplastic HHV8 related diseases (in HHV8 primary infections and high viral loads); (2) Detect active HHV8 replication; and And (3) monitor response to treatment in post-transplant patients with HHV8 related diseases Issue of serological assays in HHV8 diagnosis: Lack of any serological gold standard assay Direct detection of HHV8 (HHV8 immunohisto-chemical staining) from involved site is still gold standard for diagnosis	Strictly follow and monitor

6.Screening and Surveillance

Current Cancer Screening Recommendations for Kidney Transplant Recipients Based on Guidelines and Expert Opinions

Type of Organ	Screening Recommendations	Related Guidelines or Expert Opinions
Skin	Monthly self-skin examination and 6- to 12-monthly total body skin examination by expert physicians and dermatologists.	KDIGO 2009[40] AST 2000[45] CST 2010[42] KHA-CARI 2012[43]
Lung	For adults aged 55-79 years, annual low-dose computed tomography scans for those who have smoked 1 pack per day for 30 years or equivalent.	Extrapolation from general population guidelines.
Breast	For women aged 50-74 years, screening mammography once every 2 years.	AST 2000[45] ERPG 2002[41] KDIGO 2009[40] CST 2010[42]
Liver	Routine screening using US, with and without α-fetoprotein, every 6 months in patients with cirrhosis.	AST 2000[45] KDIGO 2009[40] CST 2010[42]
Kidney	Routine screening for kidney cell carcinoma using US is not recommended for all recipients of transplants, except for high-risk individuals.	Based on a study by Wong G et al.[44]
Colon–rectum	For adults aged 45-75 years, fecal immunochemical testing biennially, sigmoidoscopy every 5 years, or colonoscopy every 5-10 years.	AST 2000[45] ERPG 2002[41] KDIGO 2009[40] CST 2010[42]
Cervix	Annual Pap testing with HPV testing every 3-5 years starting at the age of 25 years until 74 years.	AST 2000[45] ERPG 2002[41] KDIGO 2009[40] CST 2010[42] KHA-CARI 2012[43]
Prostate	For men aged 55-69 years, screening decisions should be individualized. Men ≥70 years should not be routinely screened for prostate cancer.	AST 2000[45] ERPG 2002[41]

Recommendations for cancer screening in kidney transplant recipients

Cancer	Screening	Frequency	Guidelines
Skin and lip	Self-examination	Monthly	AST, KDIGO
		Not specified	CST/CSN, KHA-CARI, UKKA
	Examination by primary care physician or dermatologist	Annually[a]	AST, CST/CSN, KDIGO, KHA-CARI, UKKA
Cervical	Pelvic examination[b]	Every 3 yr	KDIGO, UKKA
		Annually	AST, CST/CSN, EBPG
		Not specified	KHA-CARI
	Pap smear[b]	Every 3 yr	KDIGO, UKKA
		Annually	AST, CST/CSN, EBPG
		Not specified	KHA-CARI
Colorectal	FOBT[c]	Follow general population guidelines (annually)	AST, CST/CSN, KDIGO, UKKA, EBPG, KHA-CARI
	Sigmoidoscopy[c]	Follow general population guidelines (every 5 yr)	AST, CST/CSN, KDIGO
	Colonoscopy[c]	Follow general population guidelines (every 10 yr)	AST, CST/CSN, EBPG, KDIGO, UKKA
RCC	Not recommended		AST, CST/CSN, KDIGO, UKKA, KHA-CARI
	Ultrasound[d]	Annually	EAU
		Not specified	EBPG
Prostate	Digital rectal examination[e]	Annually	AST, EBPG
		Follow general population guidelines[f]	CST/CSN, KDIGO, KHA-CARI, UKKA
	PSA[e]	Annually	AST, EBPG
		Follow general population guidelines[f]	CST/CSN, KDIGO, KHA-CARI, UKKA
Breast	Mammography[g]	1–2 yr	AST
		Follow general population guidelines	CST/CSN, KDIGO, RA, EBPG, KHA-CARI
Post-transplantation lymphoproliferative disorders	Physical examination	Every 3 mo in the first year, then annually	AST
	EBV viremia[h]	Once in the first week after transplantation, monthly for the first 3–6 mo and then every 3 mo until the end of the first post-transplant year	KDIGO, UKKA
Hepatocellular carcinoma	α-fetoprotein[i]	Annually	CST/CSN, KDIGO, UKKA
		Every 6–12 mo	AST
	Abdominal ultrasound[i]	Annually	CST/CSN, KDIGO, UKKA
		Every 6–12 mo	AST
Lung		Not recommended	AST, CST/CSN, EBPG, KDIGO, KHA-CARI, UKKA

7.Waiting time prior to renal transplant

Risk of cancer recurrence and survival in the general population and kidney transplant recipients.

	KDIGO 2020 guidelines		General population		Kidney transplant recipients	
Cancer type	Stage	Wait-time interval (years)	Incidence/mortality (global ASR[a])	5-year relative survival	Cancer recurrence	Recommendation
Breast	Early Advanced	≥2 ≥5	47.8/13.6 (female)	Localized: 99% Regional: 86% Distant: 30%	2.0 per 100 person-years (95% CI 1.3–3.3) [21][c]	Localized ≤2 years Regional ≤5 years Distant >5 years
Colorectal	Dukes' A/B	≥2	19.5/9.0[b]	Localized: 91%	4.7 per 100 person-years (95% CI 1.7–12.4)—include all GI tumours [21][c]	Localized ≤2 years
	Duke C Duke D	2–5 ≥5		Regional: 73% Distant: 15%		Regional ≤5 years Distant >5 years
Bladder	Invasive	≥2	5.6/1.9	*In situ*: 96% Localized: 70% Regional: 39% Distant: 8%	2.2 per 100 person-years (95% CI 0.2–27.0) [21][c]	*In situ*/localized ≤2 years Regional ≤5 years Distant >5 years
Kidney	<3 cm Early Large/invasive	0 ≥2 ≥5	4.6/1.8	Localized: 93% Regional: 72% Distant: 15% (includes renal pelvis)	2.2 per 100 person-years (95% CI 0.8–6.2) [21][c]	Localized ≤2 years Regional ≤5 years Distant >5 years

Risk of cancer recurrence and survival in the general population and kidney transplant recipients.

	KDIGO 2020 guidelines		General population		Kidney transplant recipients	
Cancer type	Stage	Wait-time interval (years)	Incidence/mortality (global ASR[a])	5-year relative survival	Cancer recurrence	Recommendation
Uterine	Localized Invasive	≥2 ≥5	8.7/1.8 (female)	Localized: 95% Regional: 70% Distant: 18%	0.4 per 100 person-years (95% CI 0.0–150.0) [21][c]	Localized ≤2 years Regional ≤5 years Distant >5 years
Cervical	Localized Invasive	≥2 ≥5	13.3/7.3 (female)	Localized: 92% Regional: 59% Distant: 17%	3.9 per 100 person-years (95% CI 1.6–9.3) [21][c]	Localized ≤2 years Regional ≤5 years Distant >5 years
Lung	Localized Regional/distant	2–5	22.4/18.0	Localized: 61% Regional: 34% Distant: 7%	5.4 per 100 person-years (95% CI 1.7–16.6) [21][c]	Localized/regional >5 years Distant—contraindicated
Testicular	Localized Invasive	≥2 2–5	1.8/0.2 (male)	95%	0.7 per 100 person-years (95% CI 0.2–2.3) [21][c]	Localized ≤2 years Regional ≤5 years
Melanoma	Localized Invasive	≥5 Contraindicated	3.4/0.6	Localized: 99% Regional: 71% Distant: 32%	1.9 per 100 person-years (95% CI 0.8–4.7) [21][c]	Localized ≤2 years Regional ≤5 years Distant >5 years
Prostate	Gleason ≤6 Gleason 7 Gleason 8–10	0 ≥2 ≥5	30.7/7.7 (male)	Localized: 100% Regional: 100% Distant: 32%	0.8 per 100 person-years (95% CI 0.1–12.5) [21][c]	Localized/regional ≤2 years Distant ≥5 years

Risk of cancer recurrence and survival in the general population and kidney transplant recipients.

	KDIGO 2020 guidelines		General population		Kidney transplant recipients	
Cancer type	Stage	Wait-time interval (years)	Incidence/mortality (global ASR[a])	5-year relative survival	Cancer recurrence	Recommendation
Thyroid	Stage I Stage II Stage III Stage IV	0 ≥2 ≥5 Contraindicated	6.6/0.4	Localized: 100% Regional: 98% Distant: 53%	1.8 per 100 person-years (95% CI 0.2–12.8) [21][c]	Localized/regional ≤2 years Distant >5 years
Hodgkin lymphoma	Localized Regional Distant	≥2 3–5 ≥5	1.0/0.3	Stage I: 92% Stage II: 95% Stage III: 86% Stage IV: 80%	9% [35, 36] 1.3 per 100 person-years (95% CI 0.2–10.0) [21][c,d]	Stage I/II ≤2 years Stage III/IV ≤5 years
Non-Hodgkin lymphoma	Localized Regional Distant	≥2 3–5 ≥5	5.8/2.6	Stage I: 87% Stage II: 78% Stage III: 72% Stage IV: 64%	11% [35, 36] 1.3 per 100 person-years (95% CI 0.2–10.0) [21][c,d]	Stage I Stage II/III ≤5 years Stage IV >5 years

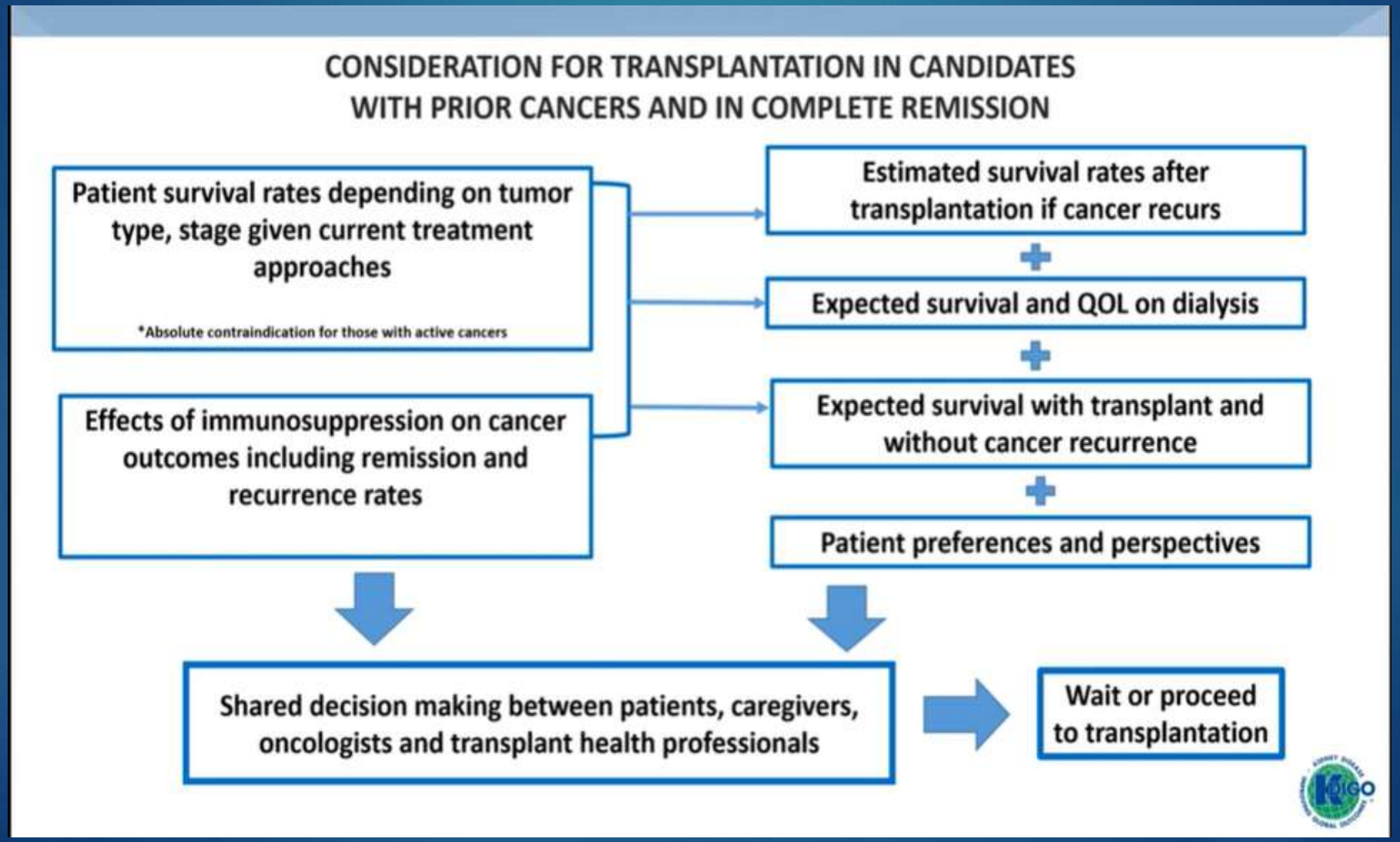
Risk of cancer recurrence and survival in the general population and kidney transplant recipients.

	KDIGO 2020 guidelines		General population		Kidney transplant recipients	
Cancer type	Stage	Wait-time interval (years)	Incidence/mortality (global ASR[a])	5-year relative survival	Cancer recurrence	Recommendation
PTLD (in kidney transplant recipients)	Nodal Extra nodal and cerebral	≥2 ≥5	Not reported	Overall survival (prior kidney transplant): 63% at 1 year, 55% at 5 years [37] 5-year survival [37]: nodal–64%; bone marrow–23%; CNS–42%; allograft–62%; other extra-nodal–49%	2.8% (7/254) after second kidney transplant (with history of PTLD) [38]	Nodal ≤5 years Extra-nodal >5 years
NMSC		No recommendation	Not reported	BCC: 100%, SCC: 95% [39] 2-year survival [40]: locally invasive SCC <25%, metastatic <10%	Geographical variation: Italy (5% after 5 years and 10% after 10 years); Northern Europe (10% after 10 years and 40% after 20 years); Australia (45% after 11 years and 70% after 20 years) [41, 42]	Localized ≤2 years Locally invasive SCC >5 years Metastatic SCC—contraindicated
Multiple myeloma		No recommendation	1.8/1.1	Localized: 79% Distant: 57%	50% [43]	
Brain		No recommendation	3.5/2.8	Localized: 35% Regional: 21% Distant: 30%	No data	

Risk of cancer recurrence and survival in the general population and kidney transplant recipients.

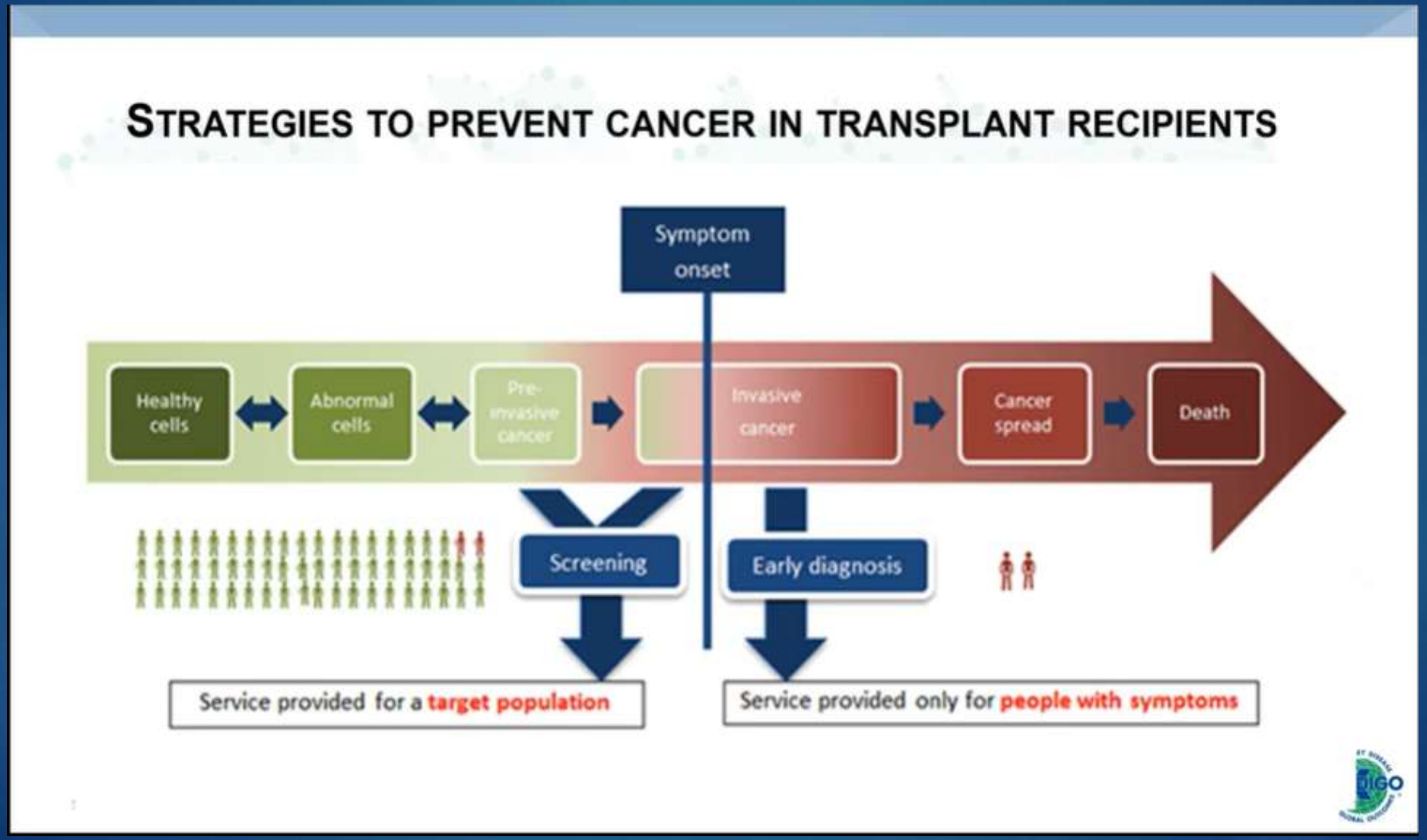
	KDIGO 2020 guidelines		General population		Kidney transplant recipients	
Cancer type	Stage	Wait-time interval (years)	Incidence/mortality (global ASR[a])	5-year relative survival	Cancer recurrence	Recommendation
Ovary		No recommendation	6.6/4.2 (female)	Localized: 93% Regional: 74% Distant: 31%	No data	Localized ≤2 years Regional ≤5 years Distant >5 years
Stomach		No recommendation	11.1/7.7	Localized: 72% Regional: 33% Distant: 6%	No data	Localized ≤5 years Regional >5 years Distant—contraindicated
Liver		No recommendation	9.5/8.7	Localized: 36% Regional: 13% Distant: 3% (includes intrahepatic bile duct)	No data	Localized >5 years Regional/distant—contraindicated
Oesophagus		No recommendation	6.3/5.6	Localized: 47% Regional: 26% Distant: 6%	No data	Localized >5 years Regional/distant—contraindicated
Lip/oral cavity		No recommendation	4.1/1.9	Lip: localized: 94%; regional: 63%; distant: 38% Tongue: localized: 84%; regional: 70%; distant: 41% Oral cavity and pharynx: localized: 86%; regional: 69%; distant: 40%	No data	
Leukaemia		No recommendation	5.4/3.3	66% (ALL: 71%, AML: 31%, CLL: 88%, CML: 70%)	No data	

Consideration for transplantation in candidates with prior cancers and in complete remission



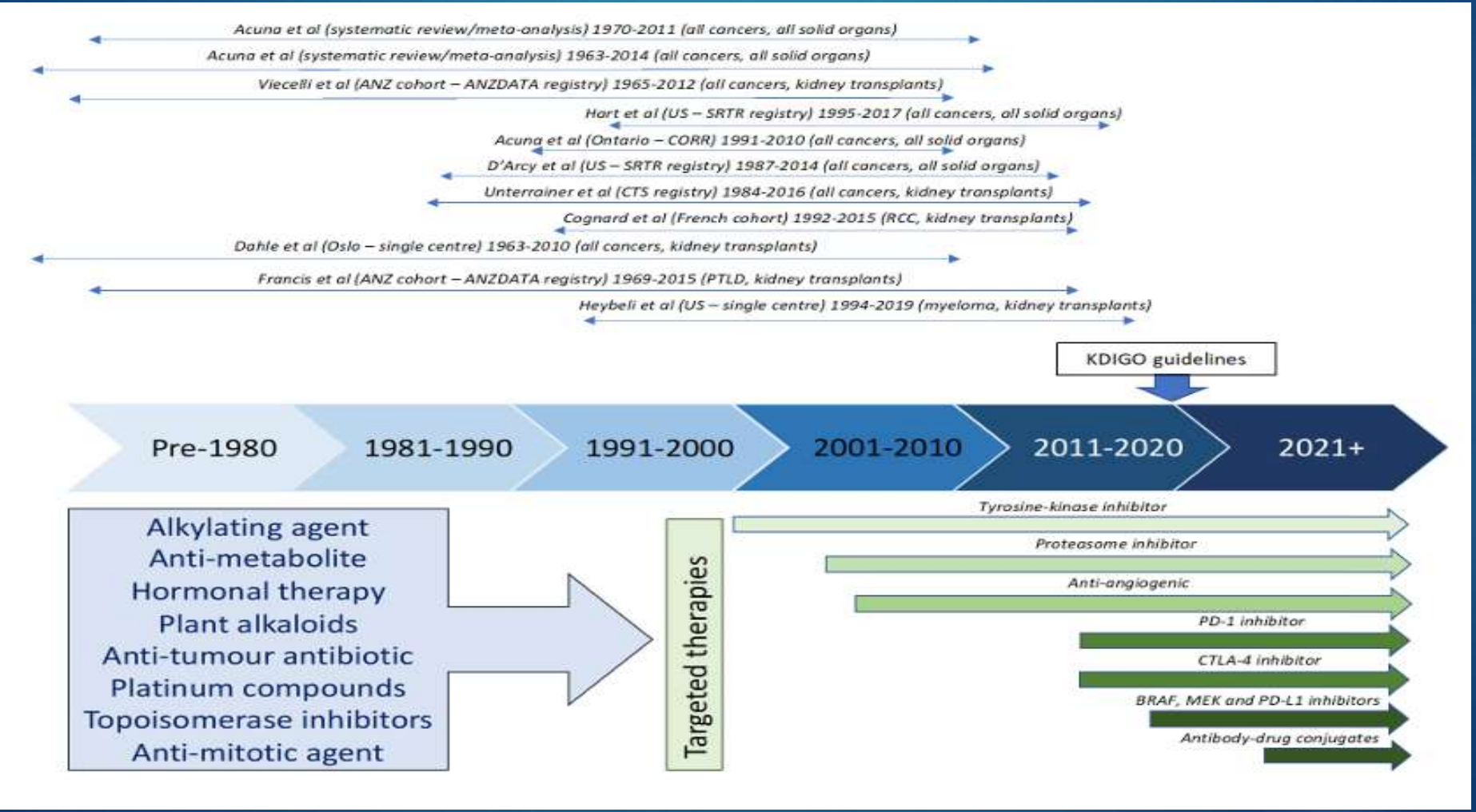
8.Management

Strategies to prevent cancer in transplant recipients

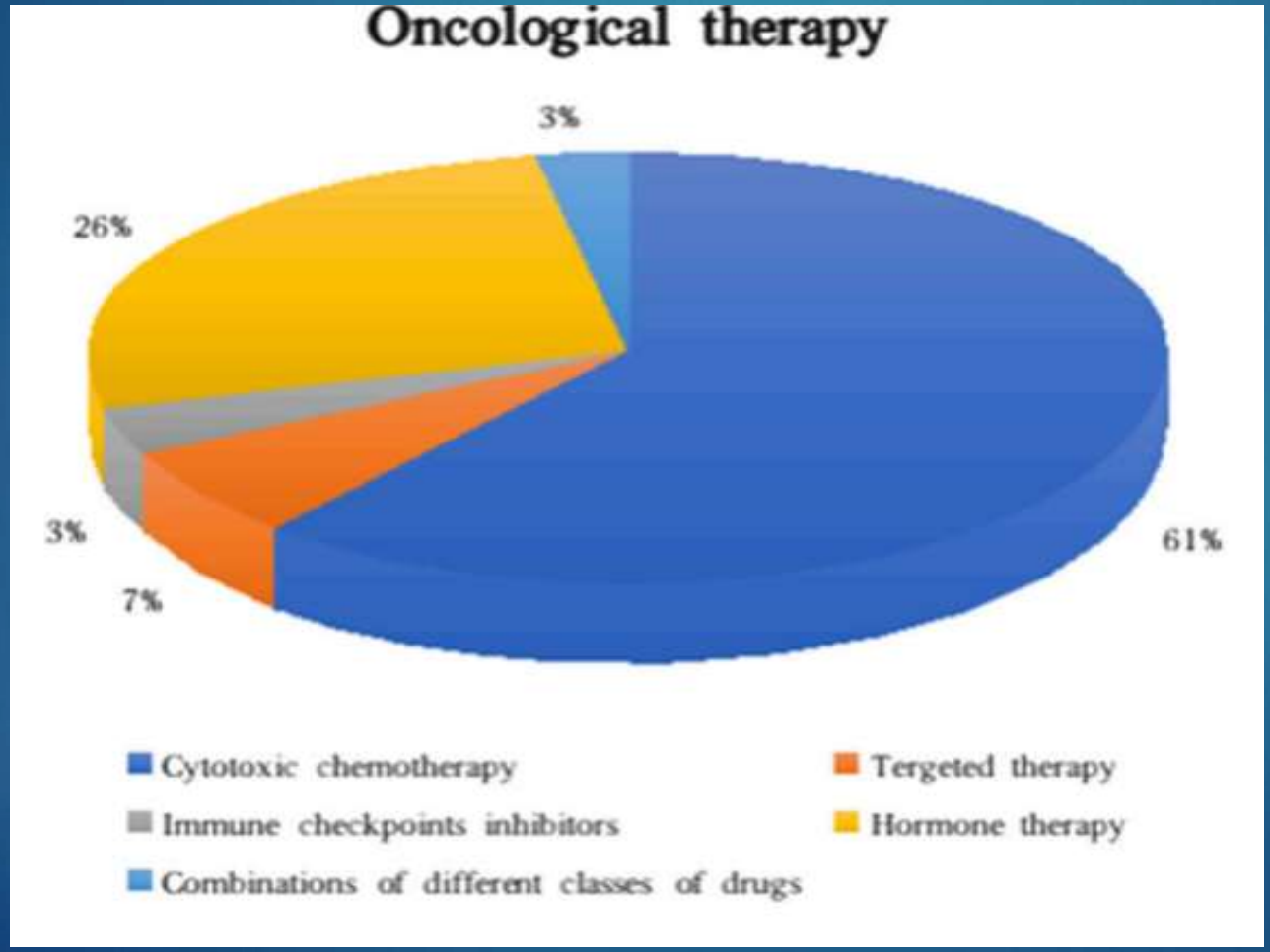


Timeline of novel anti-cancer drug approval and cohort studies of kidney transplant recipients with cancer.

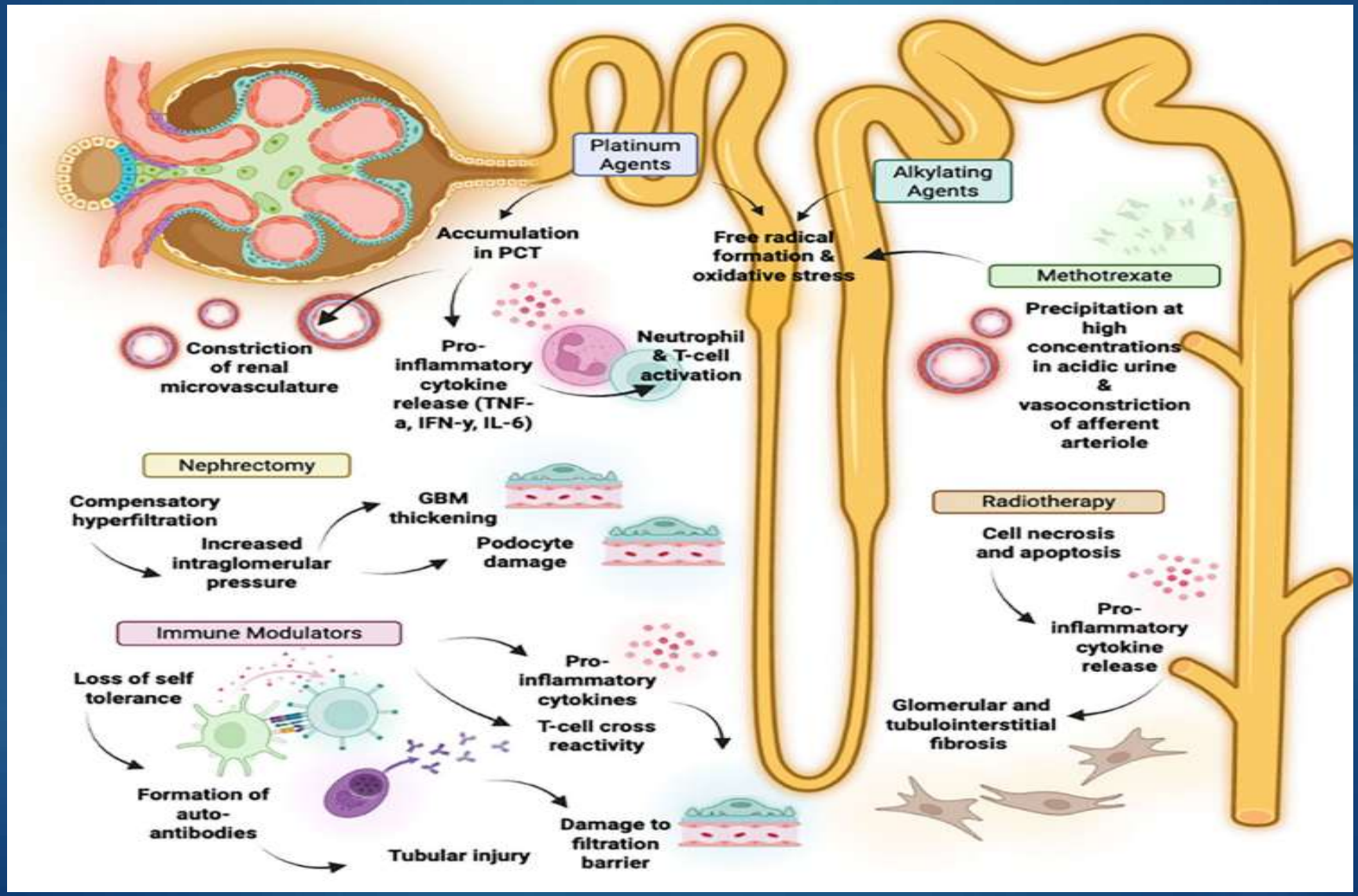
Clinical Kidney Journal , 2023, vol. 16, no. 11, 1908–1916



Therapeutic Strategies for Cancer After KTx: Oncological Treatment



Mechanisms of kidney injury in cancer therapy



Cancer therapy-specific strategies for preventing kidney injury

Cancer therapy	Mechanism of kidney injury	Kidney injury prevention strategies	Mechanism of injury prevention
Cisplatin	Pro-inflammatory cytokine release, PMN and T-cell recruitment Oxidative stress Vasoconstriction of renal microvasculature	Hyperhydration ± furosemide	Improves renal clearance of drug, prevents drug accumulation that leads to inflammatory response
		Sodium chloride (0.9% NaCl)	Exact mechanism is unknown. Change in osmolarity may trigger cellular stress response that modulates sensitivity to cisplatin and limits nephrotoxicity [80]. Higher IC chloride levels may prevent cisplatin hydrolysis and minimize oxidative stress caused by toxic metabolites [81]
		Magnesium sulfate	Likely reduces tubular cisplatin accumulation, oxidative stress and tubular injury
		Acetazolamide	Alkalinizes urine which improves cisplatin metabolite clearance. Anti-inflammatory effect through inhibition of prostaglandin synthesis. Antioxidant properties reduce oxidative stress [82]
Cyclophosphamide/ Ifosfamide	Oxidative stress	Hyperhydration, frequent bladder emptying	Improves renal clearance of drug metabolites and minimizes contact time with urothelium
		Mesna	Binds acrolein (urotoxic metabolite) to prevent hemorrhagic cystitis and secondary obstructive uropathy
High-dose methotrexate	Afferent arteriolar vasoconstriction Tubular precipitation causes free radical formation and oxidative stress	Hyperhydration	Improves renal clearance of drug, prevents precipitation in renal tubules
		Leucovorin (folinic acid)* *Folate analogue*	Restores pool of folate metabolites used for DNA synthesis to reduce systemic effects of HDMTX
		Glucarpidase *Recombinant zinc-dependent metallopeptidase*	Cleaves methotrexate into non-toxic metabolites. FDA approved single-dose rescue for children with serum MTX level ≥ 1 mmol/L. Reduces MTX levels by up to 99% within an hour
Radiotherapy	Oxidative stress RAAS activation	Limit total RT dose *< 10–15 Gy*	Limits exposure
Nephrectomy *Complete or partial*	Compensatory hyperfiltration of remaining nephrons, podocyte damage and GBM thickening	Patient education *Counseling on single kidney health risks and avoidance of nephrotoxic drugs (i.e., NSAIDS)*	Reduces incidence of future episodes of AKI and delays onset of CKD

Transplant Onconephrology in Patients with Kidney Transplants

ACKD
Advances in Chronic Kidney Disease

Pretransplant wait-time post-malignancy

- Wait times are based on 5-year survival rate of ≥ 80%
- Wait time duration is 0-5 years depending on disease grade

Cancer screening post-transplant

- Post-transplant cancer occurs at 2x standard incidence

Screening Recommendations:

- Age-appropriate surveillance
- Exception: Yearly skin cancer screening

Immunosuppression & cancer risk

Mechanisms of increased cancer risk include

- Reduced immune surveillance
- Impaired defense against oncogenic viruses
- Drug specific pathways

Cancer treatment post-transplant

- Dose adjustment may be indicated based on kidney function
- Be aware of associated adverse events & antineoplastics contraindicated in transplant

The changing landscape of malignancy subpopulations

- PTLD: Emerging therapies in refractory disease (CAR-T, EBV-CTL)
- MM: Emerging strategies with kidney transplant in low-risk disease post-ASCT

PTLD, post-transplant lymphoproliferative disorder; MM, multiple myeloma; EBV-CTL, EBV-directed cytotoxic T cell therapy; ASCT, autologous stem cell transplant

Reference: Murakami N et al. ACKD. 2022

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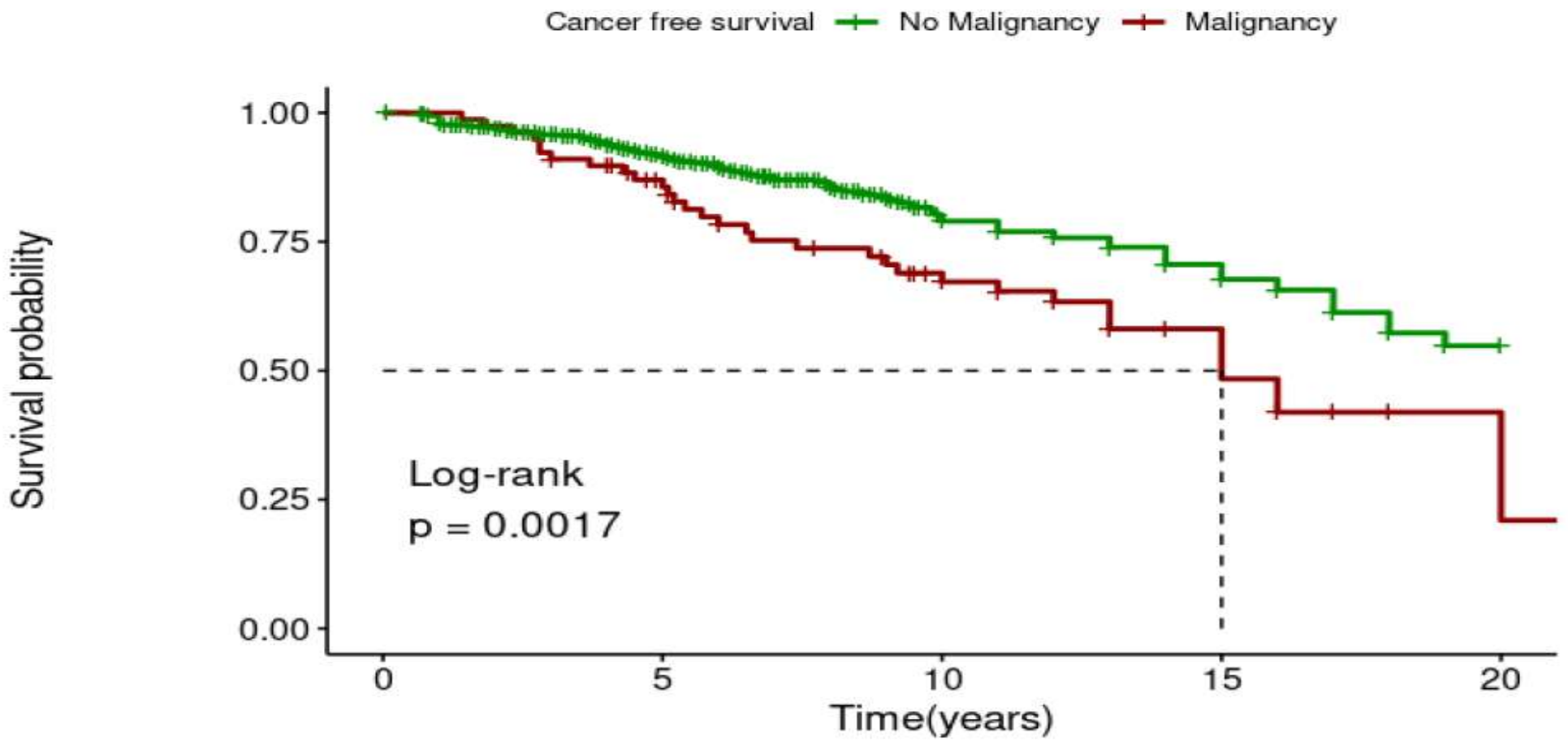
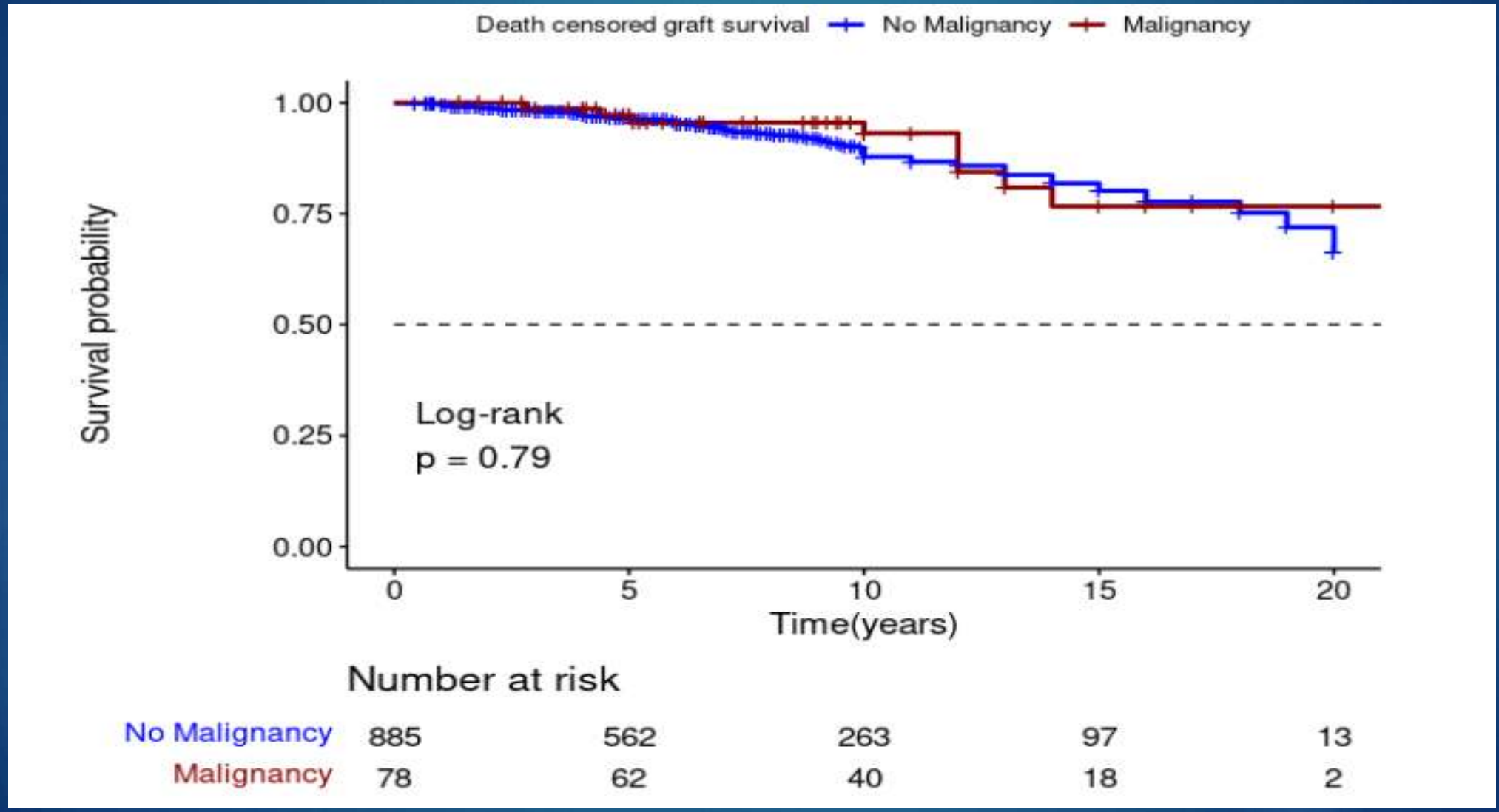
Conclusion: With emerging novel cancer treatments, it is critical to have multidisciplinary discussions involving patients, caregivers, transplant nephrologist and oncologists to achieve patient-oriented goals.

9.Outcomes and Prognosis

Outcome of de novo post-transplant malignancy on recipient survival.



Effect of de novo post-transplant malignancy on death-censored graft survival.



Prognosis

Cancer Type	Prognostic Outlook
Renal Cell Carcinoma (RCC)	Generally **good** if detected early in native kidneys; 5-year survival rates are 68%–97%.
Non-Melanoma Skin Cancer	High incidence but **low mortality**, though they tend to be more aggressive and recurrent than in the general population.
Kaposi Sarcoma	Often **regresses** with reduction of immunosuppression or switching to mTOR inhibitors like sirolimus.
PTLD	**Poor prognosis** with a median time from diagnosis to death of roughly **6 months**, though survival has improved recently with rituximab-based therapies.
Melanoma	High mortality; history of pre-transplant melanoma is the strongest risk factor for poor outcomes.

Key Factors Influencing Prognosis

- **Immunosuppression Management:** The "cornerstone" of treatment is reducing immunosuppression to allow the body's immune system to fight the cancer. However, this carries a high risk of **graft rejection and loss**.
- **Patient Age:** Older age at both the time of transplant and cancer diagnosis is a significant predictor of worse survival.
- **Cancer Stage at Diagnosis:** Approximately **40% of solid organ cancers** in transplant recipients are already at an advanced stage (lymph node-positive or metastatic) when discovered.
- **Type of Immunosuppressant:** Switching from calcineurin inhibitors (CNIs) to mTOR inhibitors (e.g., sirolimus) has shown promise in reducing the progression of certain cancers, particularly skin cancers and Kaposi sarcoma.

Conclusions

- Malignancy is one of the most common causes of death in kidney transplant recipients.
- In general, the cancer incidence in solid organ transplant recipients is increased 2- 4 fold compared with the general population.
- Moreover, cancer-related mortality rates are also higher in solid organ transplant recipients compared with the general population
- Several risk factors for post-transplantation cancer development have been identified and immunosuppression is considered the most important risk factor, as it decreases the immunologic control of oncogenic viral infection and immunosurveillance.


THank
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