Biologics in Vulnerable Populations

Vaccinations

For all biologics:

- ✓ Vaccinate all patients receiving biologics and DMARDS for ***influenza*** and ***pneumococcus***; vaccines are safe and efficacious (grade II evidence)
- ✓ Vaccinate high risk patients for ***hepatitis B***; vaccines are safe and efficacious (grade IV evidence)
- ✓ Administer ***inactivated vaccines*** prior to starting treatment with methotrexate/DMARDs; vaccines remain safe but *may no longer be efficacious* (grade I evidence)
- ✓ Administer ***live attenuated vaccines*** 4 weeks prior to beginning therapy with biologics. If vaccine is otherwise indicated, suspend treatment with biologics then administer vaccine after appropriate delay (there is consensus that 4 weeks is safe); *vaccines may not be safe or efficacious* (grade IV evidence)

For methotrexate:

- ✓ Vaccinate patients with RA, age 60 or over, for ***Herpes zoster*** at physician discretion; vaccine is safe (at ≤ 25mg methotrexate weekly) and efficacious (grade IV evidence)

Table 7. Summary of CRA recommendations for vaccination in patients with rheumatoid arthritis (RA) (Recommendations 7–9).

	Inactivated/Killed Vaccines			Live Attenuated Vaccines	
	Influenza (annual)	Pneumococcal (booster after 3-5 yrs)	Hepatitis B	Herpes Zoster	Other
Methotrexate*	✓	✓	✓†	✓††	Caution
Leflunomide	✓	✓	✓†	✓††	Caution
Sulfasalazine	✓	✓	✓†	✓††	Caution
All biologics	✓	✓	✓†	Avoid	Avoid

✓ Recommended; ideally administer prior to initiating therapy. † Recommended in high-risk groups including residents, travelers or close contact with individuals from hepatitis B endemic areas, illicit drug users, persons engaging in risky sexual behaviors/history of sexually transmitted infection, men who have sex with men, chronic liver disease, occupational exposures, frequent blood transfusions. †† Recommended in RA patients > 60 years old. * Methotrexate ≤ 25 mg per week.

Hepatitis+

For all biologics:

- ✓ Patients should be screened for hepatitis B/C status before starting therapy with any ***biologic or methotrexate*** (grade III evidence)
- ✓ Safety profile of biologics in patients with chronic infection (hep B/C) is not yet sufficiently well understood (no evidence)
- ✓ For high-risk populations, please see section on vaccination

Malignancy+

For all biologics:

- ✓ Consult with an oncologist in the event of an active conflict between biologic therapy for RA and active malignancy. General consensus recommends withholding biologic therapy while the patient is receiving chemotherapy or radiotherapy (grade IV evidence)
- ✓ ***Anti-TNF*** should be used with *caution/avoided* in patients with a history of malignancy, as there is some evidence of increased risk (grade IV evidence)

For patients with a history of lymphoma:

- ✓ ***Hydroxychloroquine***, ***sulfasalazine***, and ***rituximab*** are *appropriate* biologic options (grade II evidence)
- ✓ ***Anti-TNF, methotrexate*** therapy should be *avoided* (grade IV evidence)
- ✓ ***Abatacept, tocilizumab*** should be used *with caution*, ideally after consult with an oncologist (no evidence)

For patients with a history of non-melanoma skin cancer:

- ✓ ***Hydroxychloroquine***, ***sulfasalazine***, ***leuflunomide, and methotrexate*** are *appropriate* therapeutic options (grade II evidence)
- ✓ ***Anti-TNF*** therapy should be avoided (grade IV evidence)
- ✓ ***Abatacept, tocilizumab, and rituximab*** should be used *with caution*, ideally after consult with an oncologist (no evidence)

For patients with a history of solid tumors:

- ✓ ***Hydroxychloroquine***, ***sulfasalazine***, ***leuflunomide, and methotrexate*** are *appropriate* therapeutic options (grade II evidence)
- ✓ ***Anti-TNF*** therapy should be avoided in patients with melanoma only; there is no compelling consensus of increased risk of other types of solid tumor malignancy (grade IV evidence)
- ✓ ***Abatacept, tocilizumab, and rituximab*** should be used *with caution*, ideally after consult with an oncologist (no evidence)

Table 8. Summary of CRA recommendations regarding treatment with traditional and biologic disease-modifying antirheumatic drugs (DMARD) in rheumatoid arthritis (RA) patients with malignancy (Recommendations 10–13).

	Option	Use with Caution (risk unknown/ no evidence)	Use with Caution (some evidence of increased risk)
Active malignancy, receiving cancer chemotherapy/radiation.	*	*	*
History of malignancy			
Lymphoma	Sulfasalazine, hydroxychloroquine, rituximab	Abatacept, tocilizumab	Methotrexate, anti-TNF
Nonmelanoma skin cancer	Methotrexate, leflunomide, sulfasalazine, hydroxychloroquine	Abatacept, rituximab, tocilizumab	Anti-TNF
Solid tumor	Methotrexate, leflunomide, sulfasalazine, hydroxychloroquine	Abatacept, rituximab, tocilizumab	Anti-TNF (melanoma)

* Treatment decisions should be made on a case-by-case basis in conjunction with a cancer specialist and the patient. Anti-TNF: anti-tumor necrosis factor.

Resources

Bykerk, V. P.et al. (2012). Canadian Rheumatology Association recommendations for pharmacological management of rheumatoid arthritis with traditional and biologic disease-modifying antirheumatic drugs. *The Journal of Rheumatology*, *39*(8), 1559-1582.

Vassilopoulos, D., & Papatheodoridis, G. V. (2012). The safety of anti-TNF therapy in patients with hepatitis B and C virus infection. *International Journal of Clinical Rheumatology*, *7*(2), 191-196.